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TITLE: IBMISPS (International Brain Mapping & Intraoperative Surgical Planning Symposium)

PRINCIPAL INVESTIGATOR: Babak Kateb

CONTRACTING ORGANIZATION: International Brain Mapping & Intraoperative Surgical Planning Society
West Hollywood, California 90046

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PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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Babak Kateb

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The second annual meeting of International Brain Mapping & Intra-operative Surgical Planning Society (IBMISPS) was held In LA. The association is organized for the purpose of encouraging leading basic and clinical scientists who are interested or active in areas of Brain Mapping (BM) and intra-operative Surgical planning (ISP) to share their findings with other physicians and scientists across the disciplines. Currently, there is no combined conference on both subjects. This symposia intends to build a bridge between the two fields for next 5 years. The meeting will be organized by the board of directors and who will form the organizing committees: Search, Medical Education Committee, Program and Finance. The event will have significant clinical and basic science components. Thus, it will be a multidisciplinary venue to explore and clarify a defined subject, problem, or area of knowledge related to BM and ISP with leaders in the field. IBMISPS is set for Nov. 17-19 in Los Angeles in order to avoid any conflict with other major neurosurgical, radiological and neuroscieties/association/Conferences. IBMISPS is also intended for the purpose of promoting the public welfare through the advancement of Intraoperative Surgical Planning and Brain Mapping, by a commitment to excellence in education, and by dedication to research and scientific discovery. The mission of the association will be achieved through a multi-disciplinary collaboration of government agencies, patient advocacy groups, educational institutes and private sector (industry) brought together in order to address issues and problems related to BM and ISP and implement new technologies to benefit patient care. We had specific scientific sessions on ranging from Image Guided Surgery to Neuromathematics & informatics. All talks and abstracts that are presented in the symposium will be published in a peer review journal. Travel award to an outstanding student, residents, women and minorities will be also dedicated.

15. SUBJECT TERMS
Brain mapping, Image Guided Surgery, Intraoperative Surgical Planning, IBMISPS

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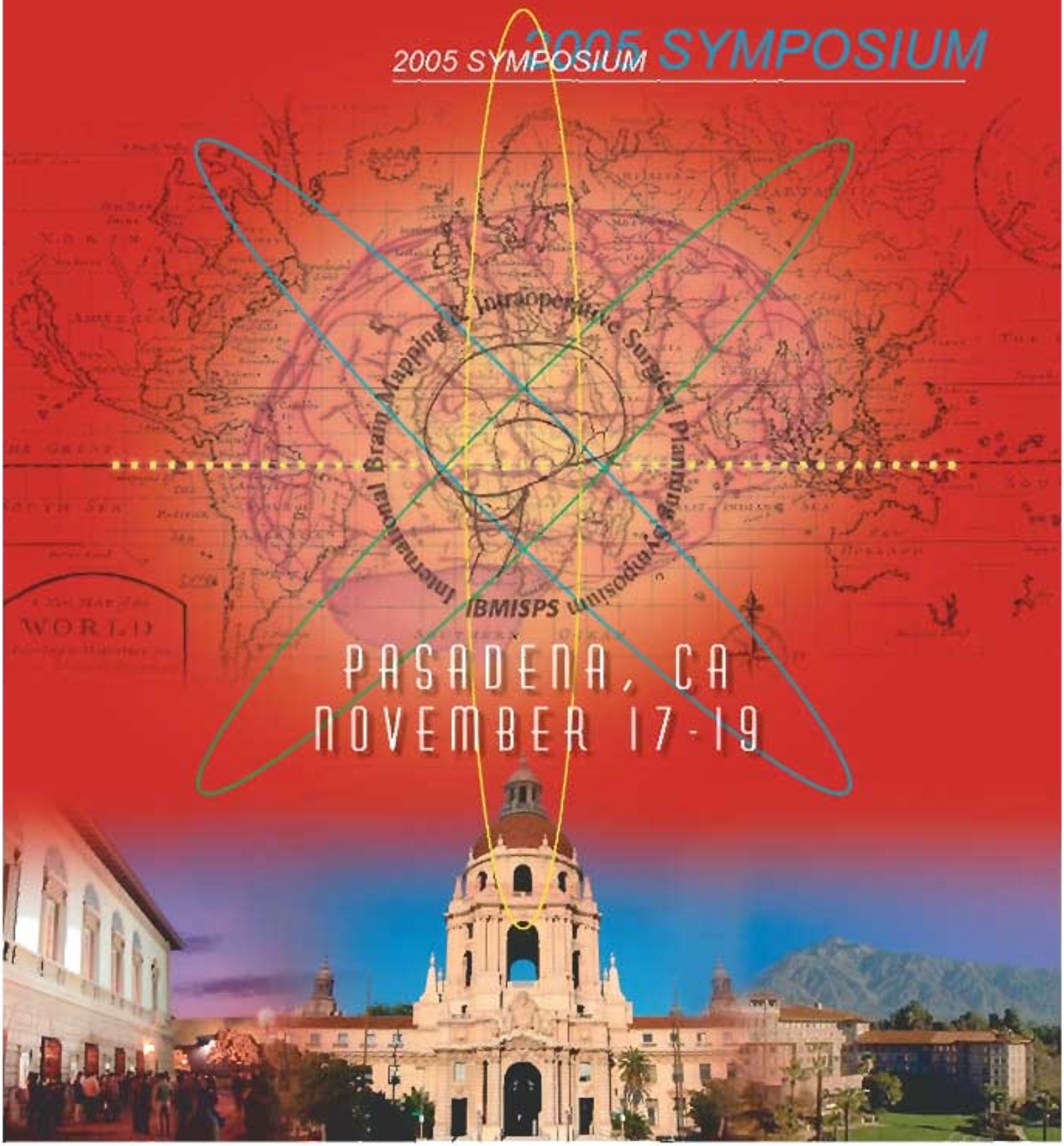
International Brain Mapping and Intraoperative Surgical Planning Society

2005 SYMPOSIUM



PASADENA, CA
NOVEMBER 17-19

President's Address

Ferenc A. Jolesz, M.D.
President, IBMISPS
Member of National Academy of Science
of the US and Hungary

It is my pleasure to invite physicians, scientists, colleagues and friends to the second annual meeting of International Brain Mapping and Intraoperative Surgical Planning Symposium (IBMISPS) in the city of Pasadena, California in November 17-19 2005.

The 2005 symposia's theme is "integrating technology & medicine" with a promise to introduce the state-of-the-art basic and clinical research directions as well as special subject matters on current issues on stem cell and prosthetics ethics.

In addition to image guided surgery and its application in intraoperative brain mapping the topics of 2005 IBMISPS will include other related research areas ranging from molecular and cellular imaging, nanoscience and genomics. The meeting objective is to create a unique scientific and educational environment for the participants and facilitate the exchange of ideas among different disciplines such as engineering, physics, neuroscience and neurosurgery.

The program committee of IBMISPS has assembled a dedicated team of scientists, physicians and surgeons to achieve the highest standard of scientific and educational quality. We are specially honored to host the honorable US Senator Barbara Boxer of California who will deliver the welcoming message. She will receive Excellence in Research, Development and Education Crystal Award for her significant contributions to the healthcare, research and education from IBMISPS.

This year again we will express our appreciation to leading companies for their contribution to the field and patient care as well as Ms. Soraya Khalilian who has shown extraordinary courage and dedication in the care of her son who is suffering from a rare brain tumor. The awards will be presented in the Award Banquet that is scheduled for Friday November 18th 2005.

As the first president of IBMISPS, I would like to welcome you and your family to this special scientific event.

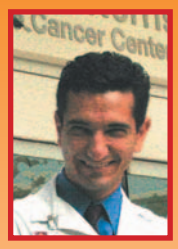
Ferenc A. Jolesz, M.D.
President, IBMISPS
Member of National Academy of Science
of the US and Hungary

IBMISPS – Mission Statement

IBMISPS is a non-profit association organized for the purpose of encouraging basic and clinical scientists who are interested or active in areas of Brain Mapping (BM) and Intra-operative Surgical Planning (ISP) to share their findings with other physicians and scientists across the disciplines: (ie: neurosurgeons, radiologists, neurologists, biotechnologists, anthropologists and neuroscientists).

This association is also intended for the purpose of promoting the public welfare through the advancement of Intra-operative Surgical Planning and Brain Mapping, by a commitment to excellence in education, and by dedication to research and scientific discovery. The mission of the association will be achieved though a multi-disciplinary collaboration of government agencies, patient advocacy groups, educational institutes and private sector (industry) brought together in order to address issues and problems related to BM and ISP and to implement new technologies to benefit patient care.

Founder's Address



Babak Kateb
Founder, Executive Director of IBMISPS and its Foundation IBMISPF

It is a great privilege to welcome you to the annual meeting of IBMISPS. I would like to congratulate the board of directors of the Foundation and the Society for working relentlessly to establish this unique, independent and multidisciplinary biomedical association.

2005 marked the birth of IBMISPS and its foundation. The Society was created to encourage basic and clinical scientists interested in the areas of Brain Mapping (BM) and Intraoperative Surgical Planning (ISP) to share their findings with other physicians and scientists across the disciplines.

The association and foundation intend to promote public welfare through the advancement of Intraoperative Surgical Planning and Brain Mapping - with a commitment to scientific discovery through research and excellence in education.

The association will achieve its mission by bringing together members of government agencies, patient advocacy groups, educational institutes, and the private sector to address problems related to BM and ISP and implement new technologies to benefit patient care.

The birth of IBMISPS occurs at a time when the fields of Brain Mapping and Image Guided Surgery are expanding rapidly. Thus, IBMISPS is proud to have brilliant scientists, physicians, surgeons and students, who will undoubtedly contribute to the quality of science and patient care in the new millennium through an interdisciplinary approach and by a commitment to the highest ethical standards.

Babak Kateb
Founder, Executive Director of
IBMISPS and IBMISPF

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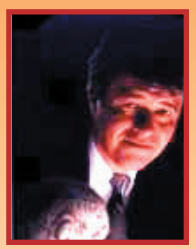

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	CONFERENCE ROOM 1 FOUNTAIN ONE	CONFERENCE ROOM 2 FOUNTAIN TWO	FOUNTAIN THREE	EXHIBITION HALL
7 AM				
8 AM	Welcome & Introduction			
9 AM	Scientific Session I: Intraoperative Surgical Planning		Poster Session I 7:00 AM - 12:00 PM	EXHIBITS 8:30 AM - 5:30 PM
10 AM	Q & A Session			
	COFFEE BREAK			
11 AM	Scientific Session II: Mapping of Brain Lesions			
12 PM	Section 2 Q & A Session		Discussion	
1 PM	LUNCH			
2 PM	Scientific Session III: Functional Brain Mapping		Poster Session II 1:00 PM - 5:00 PM	
3 PM	Section 1 Q & A Session			
	COFFEE BREAK			
4 PM	Scientific Session IV: Brain Mapping and Intraoperative Surgical Planning Using Endoscopy			
5 PM			Discussion	
6 PM	Q & A Session			

Continental Breakfast: 7:00 – 8:00 AM Every Day

	CONFERENCE ROOM 1 • FOUNTAIN 1	CONFERENCE ROOM 2 • FOUNTAIN 2
8:00 - 8:20 AM	Babak Kateb Founder and Executive Director of IBMISPS and its Foundation (IBMISPF) *Welcome & Introduction*	
8:20 - 8:30 AM	The Honorable US Senator Barbara Boxer *Welcome Message*	
8:30 - 10:25 AM	***Scientific Session I:*** ***Intraoperative Surgical Planning***	
8:30 - 8:50 AM	Chair: Professor Ferenc Jolesz, M.D. Harvard Medical School, President of IBMISPS *Intraoperative Surgical Planning*	
8:50 - 9:10 AM	Co-Chair: Keyvan Farahani, Ph.D. Program Director, Cancer Imaging Program National Cancer Institute *Image-Guided Interventions*	
9:10 - 9:30 AM	Henry Hirschber, M.D., Ph.D. Professor of Neurosurgery, Rikshopital, Norway IBMISPS Board Member *Contrast Agents for Use in Intraoperative MRI*	
9:30 - 9:50 AM	Nobuhiko Hata, Ph.D. Brigham and Women's Hospital and Harvard Medical School *Computed Monitoring of Laser-Inducted Interstitial Therapy of Brain Tumor In Intraoperative MRI*	
9:50 - 10:10 AM	Behnam Badie, M.D. Director of Neurosurgery, City of Hope, IBMISPS Board Member *Role of Imaging in Surgical Management of Low-Grade Insular Gliomas*	
10:10 – 10:25 AM	15 minutes Q/A	
10:25 - 10:40 AM	15 minutes Coffee Break	
10:40 – 12:35 PM	***Scientific Session II:*** ***Mapping of the Brain Lesions***	
10:40 - 11:00 AM	Chair: Professor Jean Lemaire, M.D., Ph.D. Professor of Neurosurgery, University of Auvergne, France IBMISPS Board Member *Direct targeting in the Subthalamic Region for DBS Surgery: Spin-Offs in Brain Mapping for Functional Neurosurgery*	
11:00 - 11:20 AM	Mark Cohen, Ph.D. Professor of Psychiatry, Neurology, Radiology, Psychology and Biomedical Physics, UCLA School of Medicine *Integrative Methods in Functional Neuroimaging*	
11: 20 – 11:40 AM	Co-Chair: Chi Zee, M.D. Professor of Radiology and Neurosurgery, Director of Neuradiology at USC *Clinical Application of Diffusion Tensor Imaging*	
11: 40 – 12:00 AM	Peter Conti, M.D. Professor of Radiology, Clinical Pharmacy and Biomedical Engineering and Director of the USC Positron Imaging Science Center and Clinic *Molecular Imaging of Brain Tumors*	
12: 00 – 12:20 PM	Linda Liau, M.D., Ph.D. Associate Professor of Neurosurgery at UCLA *Image Guided Surgery and Intraoperative MRI*	
12:20 – 12:35 PM	15 minutes Q/A	
12:35 – 1:30 PM	55 minute Lunch Break with Speaker	
1:00 – 1:20 PM	Andrea K. Scott, J.D. *Ethical and Legal Parameters of Central Nervous System Repairs*	
1:20 – 1:30 PM	10 minutes Q/A	

EXHIBIT HALL
8:30 AM – 5:30 PM

FOUNTAIN ROOM 3
POSTER SESSION I
7:00 AM – 12:00 PM

	CONFERENCE ROOM 1 • FOUNTAIN 1	CONFERENCE ROOM 2 • FOUNTAIN 2
1:30 – 3:35 PM	**Scientific Session III:** **Functional Brain Mapping**	
1:30 – 1:50 PM	Chair: Manbir Singh, Ph.D. Professor of Radiology and Biomedical Engineering University of Southern California *Diffusion Tensor Imaging and Functional MRI in Brain Mapping*	
1:50 – 2:10 PM	Co-Chair: Louis Lemieux, Ph.D. Professor of Physics Applied to Medical Imaging Department of Clinical and Experimental Epilepsy *Institute of Neurology, University College London* *EEG-Correlated MRI for Localization in Epilepsy*	
2:10 – 2:40 PM	SungWon Chung, Ph.D. UCSF School of Medicine *New Insight into the Role of Superior Longitudinal Faciculus*	
2:40 – 3:00 PM	Jeffery Burman, Ph.D., UCSF *Accuracy of Diffusion Tensor MRI Tractography Assessed with Subcortical Intraoperative Stimulation and Magnetic Source Imaging*	
3:00 – 3:20 PM	Heather O'Leary, B.Sc., M.S. Research Associate, Harvard Medical School *Design of Neuro-feedback Software Using Trial-Based Functional MRI on Motor Imagery*	
3:20 – 3:35 PM	15 minutes Q/A	
3:35 – 3:50 PM	15 minutes Coffee Break	
3:50 – 5:35 PM	***Scientific Session IV:*** ***Brain Mapping and Intraoperative Surgical Planning Using Endoscopy***	
3:50 – 4:10 PM	Chair: John Frazee, M.D. Professor of Neurosurgery Director of Neuroendoscopy at UCLA *Advance Neuroendoscopy: Present and Future*	
4:10 – 4:20 PM	Co-Chair: Warren Grundfest, M.D. Professor of Surgery and Biomedical Engineering UCLA, VP IBMISPS and Board Member *The Trans-Blood Vision Imaging System*	
4:20 – 4:40 PM	Marvin Bergesnieder, M.D. Associate Professor of Neurosurgery Co-Director of Neuroendoscopy at UCLA *Two-Port Endoscopic Microsurgical Excision of Colloid Cysts*	
4:40 – 5:00 PM	Tien T Nguyen, M.D. Assistant Professor of Neurosurgery *Intraoperative Planning for Endoscopic Management of Hydrocephalus*	
5:00 – 5:20 PM	David A Feinberg, Ph.D., M.D. President and CEO, Advanced MRI Technologies, LLC Adjunct in Departments of Radiology and Physics, Washington University and Mallinckrodt Institute, St. Louis *Dynamic MR Angiography and Blood Flow Measurements in Arteriovenous Malformations, Cerebral Aneurysms and Atherosclerotic Disease the Vanguard of Neuroendoscopy: A Challenge*	
5:20 – 5:35 PM	15 minutes Q/A	
5:35 – 5:50 PM	15 minutes Wine & Cheese Break	
6:00 – 6:30 PM	**ADVISORY BOARD MEETING**	

EXHIBIT HALL
8:30 AM – 5:30 PM

FOUNTAIN ROOM 3

POSTER SESSION II
1:00 AM – 5:00 PM

IBMISPS BOARD MEETING
6:30 PM – 7:30 PM

SAN RAFAEL BOARD MEETING ROOM
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DAY TWO • NOVEMBER 18, 2005 . . . . . AT-A-GLANCE

	CONFERENCE ROOM 1 FOUNTAIN ONE	CONFERENCE ROOM 2 FOUNTAIN TWO	FOUNTAIN THREE	EXHIBITION HALL
7 AM				
8 AM	Welcome & Introduction			
9 AM	Scientific Session V: Stereotactic-Radiosurgery Planning	Scientific Session VI: Bio-Photonics and Advanced Devices	Poster Session I 7:00 AM - 12:00 PM	Exhibits 8:30 AM - 5:30 PM
10 AM	Q & A Session COFFEE BREAK	Q & A Session COFFEE BREAK		
11 AM	Scientific Session VII: New Horizons in Medicine: Informatics, Robotics and fMRI			
12 PM	Q & A Session	LUNCH		
1 PM	LUNCH			
2 PM	Scientific Session VIII: Neurophysiology: From the Lab Bench To Clinical Practive		Poster Session II 1:00 PM - 5:00 PM	
3 PM	Q & A Session COFFEE BREAK			
4 PM			Discussion	
5 PM				

AWARDS BANQUET • COCKTAILS 8:30 – 9:30 PM • DINNER & AWARDS 9:30 – 11:30 PM • RSVP

Continental Breakfast: 7:00 – 8:00 AM Every Day

	CONFERENCE ROOM 1 • FOUNTAIN 1	CONFERENCE ROOM 2 • FOUNTAIN 2
8:00 - 8:20 AM	Babak Kateb Founder, Executive Director of IBMISPS *Welcome & Introduction*	
8:20 - 10:15 AM	***Scientific Session V:*** ***Stereotactic and Radiosurgery Planning:***	**EXHIBIT HALL** **8:30 AM – 5:30 PM**
8:20 - 8:40 AM	Chair: Peter Gruen, M.D. USC, USA, IBMISPS Board Member Co-chair: Farzad Massoudi, M.D. UCLA, Massoudi Medical Group Vice President of IBMISPS IBMISPS Board Member *Framless Radiosurgical Technique and its Application in the Treatment of Trigeminal Neuralgia*	**FOUNTAIN ROOM 3** **POSTER SESSION I** **7:00 AM – 12:00 PM**
8:40 - 9:00 AM	Antonio A. F. De Salles, M.D., Ph.D. Professor of Neurosurgery Head of Stereotactic Radiosurgery at UCLA *Function of the Brain and Radiosurgery*	
9:00 - 9:20 AM	Stafford Chenery, Ph.D. Newport Diagnostic Center, Inc. *Image Manipulation and Isodose Planning Using the CyberKnife*	***Scientific Session VI:*** ***Bio-photonics & Advance Devices*** **9:30 - 11:05 AM**
9:20 - 9:40 AM	Alessandra Gorgulho, M.D. Neurosurgery Fellow at UCLA *AVM Radiosurgery and Brain Mapping*	Chair: Warren Grundfest, M.D. UCLA, VP IBMISPS, Board Member of IBMISPS *Biophotonics Technologies for Assessment of Cerebral Chemical Composition* **9:30 - 9:50 AM**
9:40 - 10:00 AM	Reinhard Schulte, M.D. Assistant Professor of Radiation Medicine Loma Linda University, School of Medicine *A System for Functional Proton Radiosurgery*	Co-Chair: Neal Prakash, M.D. Assistant Professor of Neurology at UCLA *Advances in Intraoperative Brain Mapping Using Optical Imaging of Intrinsic Signals* **9:50 - 10:10 AM**
10:00 - 10:15 AM	15 minutes Q/A	Changhuei Yang, Ph.D. Assistant Professor of Electrical Engineering and Bioengineering at Caltech *Forward Imaging Optical Coherence Tomography Imaging Probe* **10:10 – 10:30 AM**
10:15 – 10:30 AM	15 minutes Coffee Break	Steven Smith, Ph.D. Xenogen Corporation Bioluminescent Imaging in Transgenic Mouse Models of Neurological Damage and Disease **10:30 - 10:50 AM**
10:30 - 12:35 AM	**Scientific Session VII:** **New Horizons in Medicine:** **Informatics, Robotics and fMRI**	15 minutes Q/A **10:50 - 11:05 PM**
10:30 - 10:50 AM	Chair: Stephan G. Erberich, Ph.D. Director, Functional Imaging & Biomedical Informatics CHLA/USC, Assistant Professor, Radiology & Biomedical Engineering USC IBMISPS Board member, VP of IBMISPF *Grid-Based fMRI Processing Service for Clinical and Neuroscience Brain Mapping*	15 Minutes Break **11:05 – 11:20 AM**
10:50 - 11:10 PM	Co-chair: Gerhard Friehs, M.D. Associate Professor for Clinical Neurosciences (Neurosurgery) Brown University, Providence, Rhode Island *Braingate - A Human Brain-Machine Interface*	
11:10 - 11:30 AM	Theodore W. Berger, Ph.D. David Packard Professor of Engineering Professor of Biomedical Engineering and Neuroscience Director, Center for Neural Engineering *Implantable Biomimetic Electronics as Neural Prostheses for Lost Memory Function*	
11:30 - 11:50 AM	Mike Tyszka, Ph.D. Director, Magnetic Resonance Physics, Caltech Brain Imaging Center *Fact and Fiction: Artifacts in Functional Magnetic Resonance Imaging*	

	CONFERENCE ROOM 1 • FOUNTAIN 1	CONFERENCE ROOM 2 • FOUNTAIN 2
11: 50 – 12:10 AM	David J. Dubowitz, M.D. Ph.D. Assistant Professor of Radiology Associate Director, UCSD Center for Functional MRI University of California San Diego *Beyond Brain Mapping: Using fMRI to Examine Cerebral Physiology & Metabolism*	**EXHIBIT HALL** **8:30 AM – 5:30 PM**
12:10 – 12:35 AM	15 minutes Q/A	
12:35 – 1:30 PM	55 minutes Lunch Break and Speaker	**FOUNTAIN ROOM 3** **POSTER SESSION II** **1:00 PM – 5:00 PM**
12:55 – 1:15 PM	Dennis Malkasian MD PhD Clinical Associate Professor Division of Neurosurgery David Geffen School of Medicine at UCLA *Ontogenesis to Oncogenesis: Molecular Aspects and its Potential Clinical Application in Neuro-Imaging and Treatment of Brain Tumors*	
1:15 – 1:30 PM	15 minutes Q/A	
1:30 – 1:50 PM	***Scientific Session VIII: Neurophysiology: From the Lab Bench to Clinical Practice***	
1:30 – 1:50 PM	Chair: V. Reggie Edgerton, Ph.D. Professor, Vice Chair of Physiological Science; Professor of Neurobiology, Department of Molecular, Cellular, and Integrative Physiology IBMISPS Board Member *The Role of Intramuscular Strain in Generating Force in Cats and Humans*	
1:50 – 2:10 PM	Jiri Vrba, Ph.D. CTO - Chief Technical Officer, VSM Med Tech *Magnetoencephalography - A Tool for Assessment of Brain Function*	
2:10 – 2:30 PM	William Suthering, M.D. Medical Director Epilepsy & Brain Mapping Program Huntington Medical Research Institute and Huntington Hospital *MEG Spike Dipole Orientation in Temporal and Extratemporal Epilepsy*	
2:30 – 2:50 PM	Susan Bookheimer, Ph.D. Professor Dept Psychiatry and Biobehavioral Sciences UCLA School of Medicine, Ahmanson Lovelace Brain Mapping Center *Integrating Preoperative fMRI and Awake Intraoperative Electrocortical Stimulation Mapping of Language*	
2:50 – 3:10 PM	Co-Chair: Adam M. Mamelak, M.D. Neurosurgical Institute, Cedars-Sinai Medical Center IBMISPS Board Member *Magnetoencephalography Directed Surgery for Neocortical Epilepsy*	***...Awards Banquet...*** **FRIDAY, NOVEMBER 18, 2005** **IN THE MADERA ROOM-LOBBY LEVEL** **6:30 – 7:30 PM, COCKTAIL** **7:30-10:30 PM DINNER & AWARD** ***Attendance with prior RSVP only!***
3:10 – 3:25 PM	15 minutes Q/A	
3:25 – 3:40 PM	15 minutes Coffee Break	

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DAY THREE • NOVEMBER 19, 2005 · · · · · · · · · · AT-A-GLANCE

	CONFERENCE ROOM 1 FOUNTAIN ONE	CONFERENCE ROOM 2 FOUNTAIN TWO	FOUNTAIN THREE	EXHIBITION HALL
7 AM				
8 AM	Welcome & Introduction			
9 AM	Scientific Session IX: Bioethics	Scientific Session X: Vascular and Blood Flow Imaging	Poster Session I 7:00 AM - 12:00 PM	EXHIBITS 8:30 AM - 5:30 PM
10 AM	Q & A Session COFFEE BREAK	Q & A Session COFFEE BREAK		
11 AM	Scientific Session XI: Brain Mapping Neural Prosthesis and Brain Implants		Discussion	
12 PM	Q & A Session	LUNCH		
1 PM	LUNCH	Scientific Session XII: Neuroanatomy and Molecular Imaging		
2 PM	Scientific Session XIII: Neuro-Mathematics and Modeling	Q & A Session TEA RECESS		
3 PM	Q & A Session COFFEE BREAK		Poster Session II 1:00 PM - 5:00 PM	
4 PM	Scientific Session XIV: New Horizons		Discussion	
5 PM	Q & A Session			
6 PM				

DAY THREE • NOVEMBER 19, 2005 . . . . SCIENTIFIC SESSIONS

Continental Breakfast: 7:00 – 8:00 AM Every Day

	CONFERENCE ROOM 1 • FOUNTAIN 1	CONFERENCE ROOM 2 • FOUNTAIN 2	
8:20 - 9:20 AM	***Scientific Session IX: Bioethics***		
8:20 - 8:22 AM	Babak Kateb Founder and Executive Director of IBMISPS/F *Welcome & Introduction*	**EXHIBIT HALL** **8:30 AM – 5:30 PM**	
8:22 - 8:40 AM	*Shantanu Sinha Ph.D.* *Associate Professor of Radiology* *Structure-Function Correlation for the Musculo-skeletal System – an MR study*	**POSTER SESSION I** **7:00 AM – 12:00 PM**	
8:40 - 9:00 AM	J. Patrick Johnson, M.D. Director of Cedars-Sinai Institute for Spinal Disorders *Intraoperative Surgical Planning of Spine*		
9:00 - 9:20 AM	20 minute Q/A	***Scientific Session X: Vascular and Blood Flow Imaging***	9:10 – 11:05 AM
10:30 - 12:25 AM	***Scientific Session XI: Brain Mapping in Neural Prosthesis & Brain Implants***	Elizabeth Bullitt, M.D. Professor of Neurosurgery, University of North Carolina Board of IBMISPS Evaluating the Emergence of Malignancy via Measures of Vessel Tortuosity Visualized by MRA of Choroid Plexus Carcinoma in the Genetically Engineered Mouse	9:10 – 9:30 AM
10:30 - 10:50 AM	Chair: Scott Frey, Ph.D. Director, Lewis Center for Neuroimaging & Assistant Professor of Psychology University of Oregon *Amputation and Cortical Reorganization: Considerations for Neuroprosthetics*	Co-Chair: Frank P.K. Hsu, M.D., Ph.D. Professor of Neurosurgery at Loma Linda University	9:30 – 9:50 AM
10:50 - 11:10 AM	Co-Chair: Joel Burdick, Ph.D. Professor of Bioengineering at Caltech *A Miniature Robot That Autonomously Optimizes and Maintains Extra-Cellular Neural Action Potential Recordings*	Sean Armin M.D., Resident, Division of Neurosurgery Loma Linda University *Perioperative Evaluation of Cerebral Vasculature*	9:30 – 9:50 AM
11:10 – 11:30 AM	Yu-Chong Taii, Ph.D. Professor of Electrical Engineering and Bioengineering at California Institute of Technology *Flexible Parylene Neural Prosthetic Devices*	Stephen Aylward, Ph.D Director of Computer-Aided Diagnosis and Display Lab Associate Professor of Radiology, Surgery, and Computer Science University of North Carolina at Chapel Hill *Monitoring Tumor Margins During Treatment Using Automated MR to 3D Ultrasound Registration*	9:50 – 10:10 AM
11:30 - 11:50 AM	Marco Iacoboni, M.D.,Ph.D. Director, Transcranial Magnetic Stimulation Lab Ahmanson-Lovelace Brain Mapping Center Dept. of Psychiatry and Biobehavioral Sciences Semel Institute for Neuroscience and Human Behavior Brain Research Institute David Geffen School of Medicine at UCLA *The Mirror Neuron System and Intention Understanding*	Karen Tong, M.D. Assistant Professor, Radiology Dept. of Neuroradiology Loma Linda University Medical Center *CT and MR Perfusion for Assessment of Surgical Revascularization in Cerebral Ischemia*	10:10 – 10:30 AM
11:50 - 12:10 PM	Ramez Shehada, Ph.D. Research Assistant Professor Department of Biomedical Engineering University of Southern California *The Smart Drain: A Surgical Drain with Sensors*	Andreas Raabe, M.D. Associate Professor, Department of Neurosurgery Neurology and Neurosurgery Centre Johann Wolfgang Goethe University *Prospective Evaluation of Surgical Microscope-Integrated Intraoperative, Near-Infrared Indocyanine Green Video Angiography During Aneurysm Surgery*	10:30 – 10:50 AM
12:10 - 12:25 PM	15 minutes Q/A	15 minutes Q/A	10:50 – 11:05 AM
12:25 - 1:20 PM	55 minutes Lunch Break and Speaker	15 Minutes Break	11:05 – 11:20 AM
12:45 – 1:05 PM	Andrea K Scott, JD *Stem Cells And The Restoration Of Brain Function: A Hobbesian Choice*		
1:05 – 1:20 PM	15 minutes Q/A		

	CONFERENCE ROOM 1 • FOUNTAIN 1	CONFERENCE ROOM 2 • FOUNTAIN 2
1:20 – 3:15 PM	***Scientific Session XIII:*** ***Neuro-Mathematics & Modeling***	
1:20 – 1:40 PM	Chair: Vittorio Cristini, Ph.D. Associate Professor of Mathematics and Biomedical Engineering University of California, Irvine IBMISPF Board member *Computer Simulation of Cancer and Chemotherapy*	**EXHIBIT HALL** **8:30 AM – 5:30 PM**
1:40 – 2:00 PM	Vittorio Cristini, Ph. D. Associate Professor of Mathematics and Biomedical Engineering University of California, Irvine, IBMISPF Board Member *Morphologic Instability and Cancer Invasion*	***Scientific Session XII:*** ***Neuroanatomy and Molecular Imaging*** 12:40 – 2:10 PM
2:00 –2:20 PM	Co-Chair: John Sinek,Ph.D. University of California, Irvine Department of Mathematics *How Much Does Limited Tissue Penetration Affect Anticancer Drug Efficacy?*	Chair: Elaine L. Bearer, M.D., Ph.D. Professor of Medical Sciences Brown University *Mapping the Brain with Transport* 12:40 – 1:00 PM
2:20 – 2:40 PM	Hermann B. Frieboes, Ph.D. University of California, Irvine Department of Mathematics *An Integrated Computational/Experimental Model of Tumor Drug Response*	Co-Chair: Andy Obenous, Ph.D. Associate Professor of Radiation Medicine Loma Linda University *Molecular Imaging of Brain Tumors in Animal Models* 1:55 – 1:20 PM
2:40 – 3:00 PM	Valerie Trapp Department of Biomedical Engineering, UC Irvine *The Utility of Vascularized Spheroids for Modeling Angiogenesis*	Mark Schnitzer, Ph.D. Associate Professor, Stanford University School of Medicine *In Vivo Brain Imaging Using One- and Two-Photon Fluorescence Microendoscopy* 1:20 – 1:40 PM
3:00 – 3:15 PM	15 minutes Q/A	15 minutes Q/A 1:40– 1:55 PM
3:15 – 3:30 PM	15 minutes Coffee Break	15 Minutes Tea Recess 1:55 – 2:10 PM
3:30 – 5:25 PM	***Scientific Session XIV:*** ***New Horizons***	
3:30 – 3:50 PM	Chair: Shouleh Nikzad, Ph.D. Supervisor of In Situ Technology and Experiments Systems Section of NASA/JPL; Visiting Assistant Research Professor of Neurosurgery at USC, Keck School of Medicine IBMISPS Board Member *UV Imaging, Nanotechnology and Their Potential Medical Application*	**POSTER SESSION II** **1:00 PM – 5:00 PM**
3:50 – 4:10 PM	Co-Chair: Mike Barish, Ph.D. Professor and Chair, Division of Neurosciences, Beckman Research Institute of the City of Hope *Imaging of Physiological Processes in Living Brain*	
4:10 – 4:30 PM	Jim Lambert, Ph.D. Manager, Analytical Instrument Group Jet Propulsion Laboratory, California Institute of Technology *New Applications of Optical Coherence Tomography*	
4:30 – 4:50 PM	M. Amy Ryan, Ph.D. Jet Propulsion Laboratory, California Institute of Technology *Potential Applications of an Electric Nose to Medical Diagnosis and Patient Care*	
4:50 – 5:10 PM	Harish Manohara, Ph.D. Jet Propulsion Laboratory, California Institute of Technology *Nano And Micro Systems – Some Common Links Between Space and Medical Applications*	
5:10 – 5:25 PM	15 minutes Q/A	
5:25 – 5:40 PM	15 minutes Wine & Cheese Break	

This course is targeted for Scientists, Physicians, Neurosurgeons, Neurologists and Radiologists interested and/or involved in brain mapping (BM) & intraoperative surgical planning (ISP). In order to get credit, participants must attend at least one presentation and submit a credit application and evaluation form to conference staff before leaving. Participants should only claim those hours they actually attended the conference. Certificates will be mailed within 4-6 weeks after the program.

ACCME

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of Medical Education Collaborative, Inc. (MEC) and IBMISPS. MEC is accredited by the ACCME to provide continuing medical education for physicians.

Medical Education Collaborative designates this educational activity for a maximum of 21.5 category 1 credits towards the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

ANCC

Approved for 25.8 contact hour(s) of continuing education for RNs, LPNs, LVNs and NPs. This program is cosponsored with Medical Education Collaborative, Inc. (MEC) and IBMISPS. MEC is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. Provider approved by the California Board of Registered Nursing, Provider Number CEP 12990, for 25.8contact hour(s).

INSTRUCTIONS FOR CREDIT

In order to get credit, participants must attend at least one presentation and submit a credit application and evaluation form to conference staff before leaving. Participants should only claim those hours they actually attended the conference. Certificates will be mailed within 4-6 weeks after the program.

LEARNING OBJECTIVES

At the conclusion of this course, participants should be able to:

- Identify new findings in brain mapping (BM) & intraoperative surgical planning (ISP) most relevant to their own sub field (i.e.: molecular imaging and or biophotonics)
- Describe the effect of the newly developed methods in BM and ISP
- Discuss and design the possible future research and developments in BM & ISP and assess the possible impact of such research and development on their own clinical and scientific work in the future
- Describe and assess the latest cutting-edge technological advancement in BM & ISP
- Explain ways to build a bridge between the two field, BM & ISP
- Discuss and describe governmental agencies' roles in research and development of BM & ISP

Excellence in Courage and Dedication Crystal Award

Ms. Soraya Khalilian

Ms. Khalilian has dedicated the last 20 years of her life to taking care of her son, who is suffering from a very rare brain tumor. She has a sociology degree from the University of Tehran and is a retired teacher. Upon receiving the news of her son's brain tumor 20 years ago, she immigrated to the US to find a better facility to treat her son. She also went back to school and obtained her AA degree in laboratory medicine in order to better manage her son's brain tumor.

Excellence in Research, Development and Educational Support Crystal Award

Frenc A. Jolesz, MD

The IBMISPS Board of Directors is aware of Dr. Jolesz' contribution to the field such as the development and implementation of innovative image processing methods, which has brought several minimally invasive therapies into successful clinical application. He has also been credited with developing, refining, and introducing into clinical practice the idea of direct, real time MR image-guided surgical interventions as well as perfecting the use of high intensity focused ultrasound as a tissue ablation tool and integrating it with MR imaging guidance systems. Dr. Jolesz is a member of the Institute of Medicine of the National Academy of Science in the U.S. He was nominated to the National Academy of Science in Hungary in 2005. He is also the first elected president of IBMISPS.

The Honorable U.S. Senator Barbara Boxer of California

Senator Boxer is one of the Senate's leading advocates for health research. She cosponsored The National Research Investment Act of 1998 and supported subsequent appropriations that led to the doubling of funding for the NIH. Boxer is one of the nation's most outspoken advocates of research and treatment for diseases including Alzheimer's, Parkinson's Disease, ALS (Lou Gehrig's Disease) and Scleroderma.

Zeiss President Carl O'Connell

Zeiss and Siemens

Two of the leading companies in the field received the 2005 Excellence in Research, Development and Education R, D & E Crystal Award for their outstanding contributions to both the fields of Brain Mapping and Intraoperative Surgical Planning. Zeiss President O'Connell, along with Siemens President McCausland, will be receiving the Award on behalf of their companies.

TATRC

Known as one of the leading US government agancies, they received the 2005 Excellence in R, D & E award for their contribution in the feild of prosthetics and brain imaging.

Excellence in Educational Support

Codman, Siemens, Zeiss, and Medtronic
will be awarded for their contributions

This event was made possible by educational grants from the following sponsors. Thank you for your support!

GOLD LEVEL SUPPORT

United States Telemedicine and Advanced Technology Research Center (TATRC). This symposium is held in a collaborative partnership with the Telemedicine and Advanced Technology Research Center (TATRC), and is made possible by a contract administered through the U.S. Army Medical Research and Materiel Command (USAMRMC) at Fort Detrick.

EDUCATIONAL LEVEL SUPPORT

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Proceeding of 2005 Annual meeting of International Brain Mapping and Intra-operative Surgical Planning Society (IBMISPS)

Chaired by:

Babak Kateb

Founder and Executive Director of IBMISPS

President (2005-2006):

Ferenc A. Jolesz

Harvard Medical School

The Mission Statement for International Brain mapping and Intra-operative Surgical Planning Symposium (IBMISPS):

IBMISPS is a non-profit association organized for the purpose of encouraging basic and clinical scientists who are interested or active in areas of Brain Mapping (BM) and intra-operative Surgical planning (ISP) to share their findings with other physicians and scientists across the disciplines (i.e. Neurosurgeons, radiologists, neurologists, biotechnologists, anthropologists and neuroscientists).

This association is also intended for the purpose of promoting the public welfare through the advancement of Intra-operative Surgical Planning and Brain Mapping, by a commitment to excellence in education, and by dedication to research and scientific discovery. The mission of the association will be achieved through a multi-disciplinary collaboration of government agencies, patient advocacy groups, educational institutes and private sector (industry) brought together in order to address issues and problems related to BM and ISP and implement new technologies to benefit patient care.

Educational Objectives:

The event will provide participants with 27 hours of CME credit through Medical Educational Collaborative Corporation; a nonprofit organization specialized for providing CME credit for medical conferences.

Up on Competition of the scientific meeting, participants should be able to:

- Identify new findings in brain mapping (BM) & intraoperative surgical planning (ISP) most relevant to their own sub field (i.e. molecular imaging and or biophotonics)
- Describe the effect of the newly developed methods in BM and ISP
- Discuss and design the possible future research and developments in BM & ISP and assess the possible impact of such research and development on their own clinical and scientific work in the future
- Describe and assess the latest cutting-edge technological advancement in BM & ISP
  Explain ways to build a bridge between the two field, BM & ISP
- Discuss and describe governmental agencies roles in research and development of BM & ISP

<u>Specific Program</u>

Lectures
Scientific Exhibits (posters)
Special focus sessions:
Basic science
Clinical trials
Governmental regulation
Patient family
Cutting edge research and development in BM and ISP

Topics for Scientific papers

- General Issues
- Operational Issues
- Image guided systems
- Vascular & Blood flow imaging
- Intraoperative Surgical Planning & Image guided surgery
- BM and ISP in Stereotactic Radiosurgery
- Molecular and cellular imaging
- Anatomy
- Nanoscience, genomics, computational genetics in brain mapping
- 4D, Neuro-mathematics and bio-informatics
- Neurophysiology
- Functional brain mapping (fMRI, PET, ..)
- Brain Mapping and Intra-operative Surgical Planning using Endoscopy
- Biophotonics
- Brain Mapping Neural Prosthesis & Robotics
- Multi-modality imaging
- Perfusion Imaging, micromagnetic resonance imaging,
- Magnetic resonance Spectroscopic Imaging,
- high-field magnetic resonance, history of brain cartography,
- ethical issues related to the brain mapping and intra-operative surgical planning, Magnetoencephalographic,
- transcranial Magnetic Stimulation,
- Diffusion Tensor Imaging,
- SPECT functional Brain Mapping and
- histopathology in brain mapping

Mr. Babak Kateb, Founder and Executive Director of the IBMISPS chaired the 2005 annual meeting. Meeting included more than 70 speakers from 3 different continents. The congress also covered all aspects of the brain mapping and image guided surgery and created an outstanding

atmosphere for exchange of scientific data as well as formation of collaborative partnership among industry, faculties of educational institutions, patient advocacy groups and government agencies.

The following are the names, titles, topics and talks/abstracts that were presented in the 2005 congress:

First Day: Nov 17th

Scientific Session I:
Intraoperative Surgical Planning

Chair: Ferenc A. Jolesz, MD
Title: Professor of Radiology, Member of Institute of Medicine of National Academy of Science of the US and Hungary, 2005-2006 IBMISPS President
Institution: Harvard Medical School, President of IBMISPS
Time: 8:30 – 8:50 AM
Topic & Abstract:
Intraoperative Surgical Planning

Along with recent advances in minimally invasive surgery, the introduction of new imaging modalities, and the availability of high performance computing, the field of image-guided therapy (IGT) has developed at an impressive rate. Indeed, IGT has already changed the fundamentals of traditional surgery by replacing and/or complementing direct surface based visualization with volumetric information. This new approach not only represents a technical challenge but also a transformation from conventional hand-eye-coordination to interactive, navigational operations, perhaps best defined as the presentation of multi-modality-based images merged into a single model in which anatomy and pathology are at once distinguished and integrated into the same intuitive framework.

Currently, new, highly innovative technology, which optimizes and simplifies morphologic and correlated functional data derived from various imaging modalities, has been introduced into the interventional suites and operating room (OR). However, the active use of IGT is restricted in both

scope of procedures and sites of implementation. The long-term goals of improving interventional and surgical procedures and attendant outcomes, reducing costs, and achieving broad utilization can be achieved with a three-pronged approach: 1.) Improving the presentation of pre-operative and real-time, intraoperative image information 2.) Integrating imaging and treatment related technology into therapy delivery systems and 3.) Testing the clinical utility of image guidance in surgery and cancer therapy.

There are several factors, which promote image guidance techniques (IGT), including improved medical outcomes, shorter hospitalization (from the patient's perspective) and improved quality and speed of the procedures, with fewer complications (from the physician's perspective). There also describe several economic and practical barriers to the large-scale use of IGT. Many technical approaches have been followed to increase this benefit/cost ratio, including improved planning, more localized and less invasive treatment devices, and better methods to position therapy end-effectors.

Co-chair: Keyvan Farahani, Ph.D.
Title: Program Director Cancer Imaging Program
Institute: National Cancer Institute, Image-Guided Interventions
Time: (8:50 - 9:10 AM)
Topic and Abstract:
Presented Over View of the NCI and its activities
Abstract is not available.

Speaker: Henry Hirschberg MD,PhD
Title: Professor of Neurosurgery
Institution: Department of Neurosurgery, Rikshospitalet, Oslo, Norway
Time: 9:10 - 9:30 AM
Topic & Abstract:
Contrast Agents for use in Intraoperative MRI

Introduction
Surgically induced blood-barrier injury resulting in non-tumor related gadolinium enhancement has been described in several studies employing either MRI or

intraoperative CT. Intraoperativly this type of contrast enhancment might be mistaken for residual tumor thus leading to unnecessary resection. Comparison with preoperative scans, including analysis of the location and shape of the enhancement in question, although very time consuming, is often necessary. This is an underlying problem for all intraoperative iMRI systems and has led to the search for more suitable contrast agents that would be retained in tumor tissue for extended periods. This would allow for the injection of contrast at a sufficient interval prior to the initiation of surgery to allow the blood concentration of the agent to approach a low level.

Results: Ultra small superparamagnetic iron oxide particles have shown promising results as a stable single dose contrast agent for intraoperative imaging. A multifunctional nanoprobe capable of targeting glioma cells, detectable by both magnetic resonance imaging and fluorescence microscopy, has also been developed and might prove useful. No clinical series employing nanoparticles as contrast agents has been presented. Motexafin Gadolinium (MGd) is a radiation enhancer that is also detectable in vivo on MRI scans. Motexafin Gadolinium has been shown to be incorporated into tumor cells and can crosses the imperfect BBB associated with brain tumors and remain in tumor tissue for an extended period.

Conclusion: The drugs efficacy, as a radiation sensitizer, has been evaluated in several clinical series and has been well tolerated. MGd is presently being evaluated in a rodent brain tumor model.

Speaker: Nobuhiko Hata, Ph.D.
Title: Associate Professor of Radiology
Institution: Brigham and Women's Hospital and Harvard Medical School
Time: 9:30 - 9:50 AM
Topic & abstract:

Computed Monitoring of laser-inducted interstitial therapy of Brain Tumor in intra-operative MRI

[Rationale and Objective] A software for monitoring laser-inducted interstitial therapy (LITT) of brain tumor in intra-operative magnetic resonance imaging (MRI) is presented. The software is

useful for optimally ablate the tumor with integrated tumor segmentation tool and thermal monitoring tool, processing the intra-operative MR imagery on-line and real-time.
[Materials and Methods] 3D Slicer, modified specifically for LITT, gives us options to objectively measure the extent of tumor by image segmentation, mark the critical volume by thermal imaging, and update the treatment planning by comparing the original tumor lesion and treated lesion. Image segmentation was available by fuzzy-connectivity (FC) algorithm. Mapping of ablated lesion was computed from sum of thermal increase measured by thermal MR imaging. Both original tumor lesion and ablated lesion were mapped onto the T1-weighted MRI which also delineates the location of laser fiber as image void. This overlapped mapping was then used to update the treatment planning, i.e. additional laser firing or re-position of fiber, to best cover the tumor with thermal ablation.
[Results] We performed a set of retrospective study to investigate the feasibility of the software in clinical setting. A comparison of manual segmentation with those of the semi-automatic FC-based segmentation gave the average match 76%. The overlapped thermal mapping and treatment planning clearly indicated the need for re-position of the needle and subsequent laser irradiation.
[Conclusion] The system design is feasible and found useful for on-line monitoring of interstitial laser therapy.

Speaker: Behnam Badie, M.D.

Title: Associate Professor of Neurosurgery & Director of Brain Tumor Program & Director of Neurosurgery Department

Institution*:* City of Hope National Comprehensive Cancer Center

Time: (9:50 - 10:10 AM)

Topic & Abstract:

Intraoperative Resection of Brain Tumors

Surgical management of tumors involving insular cortex remains controversial. Although complex vascular anatomy and close proximity of such tumors to deep white matter tracts and eloquent cerebral cortex makes excision of insular tumors risky, aggressive removal of low-grade tumors in this area may have prognostic advantages.

We retrospectively evaluated our ten-year experience with 23 consecutive patients who underwent surgery for non-enhancing, well-circumscribed tumors involving the insular cortex. Most patients (78%) presented with new onset seizures. In 16 patients (70%) tumors involved the speech-dominant hemisphere. Mean extent of tumor resection, as calculated by volumetric MR measurement, was 85% (range: 68-100%). Only one patient developed postoperative neurological deficit (aphasia) which completely recovered within one month of surgery. The importance of

preoperative imaging (fMRI, DTI, CTA), intraoperative brain mapping, and surgical techniques for management of low-grade insular gliomas will be discussed.

Scientific session II:
Mapping of the Brain lesions

Chair: Jean Lemaire, M.D.,Ph.D.

Title: Professor of Neurosurgery

Institution: University of Auvergne, France (IBMISPS Board Member)

Time: 10:40 – 11:00 AM

Topic & Abstract:

Direct targeting in the Subthalamic Region for DBS surgery: Spin-offs in Brain Mapping for Functional Neurosurgery

Jean-Jacques Lemaire [1,6], MD, PhD, Jérôme Coste [1,5], MSc, Lemlih Ouchchane [4,6], MD, Philippe Derost [2], MD,
Miguel Ulla [2], MD, Séverine Siadoux [3], MD,
Jean Gabrillargues [3,6], MD, Franck Durif [2], MD, PhD.
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ABSTRACT: (word count = 263)

The direct targeting of subthalamic nucleus (STN) for deep brain stimulation (DBS) is a challenge. We have developed a method based on anatomical study of magnetic resonance imaging (MRI) slices (T2-weighted, cortex attenuated inversion recovery sequence; 1.5-Tesla machine)

realized in stereotactic conditions (i.e. stereotactic frame in place). The aim was to secure and to simplify the targeting as well as to provide a robust reproducibility. Preliminary clinical results have been already reported. This work focused on relationships between anatomy and electrophysiological and clinical data, collected peroperatively under local anaesthesia. Fifteen bilateral surgical procedures for severe idiopathic Parkinson's disease were studied. The stimulation parameters, i.e. the current thresholds leading benefits and adverse effects, with the clinical effects linked (efficiency on rigidity and on tremor; gaze, neurovegetative, sensitive and motor adverse effects) as well as the extra cellular recordings of neuron activity were noticed along trajectories, with respective steps of 1 mm and of 0.5 mm. Relationships were studied by a side by side analysis (30 hemispheres). Statistics was performed with SAS (v8.02, USA). We found relationships between subthalamic structures (STN and others main structures) and stimulation data, confirming the pertinence of anatomical study. The best area for DBS was the anterior dorso-lateral STN (best ratio efficiency/adverse effects). Extra cellular neuronal activity was maximum in the anterior ventro-medial STN and the adjacent substantia nigra. Beyond the surgical spin-offs, in terms of time wining and of care improvement, the direct targeting method of STN offers the opportunity to revisit stereotactic functional surgery. It also gives prospects in the domain of invasive focal treatments of brain diseases.
KEYWORDS: subthalamic anatomy, STN, direct targeting, stereotactic mapping, DBS, MRI

Stereotactic neurosurgery allows targeting of deep located structures, i.e. the basal ganglia (e.g. the subthalamic nucleus, STN), without visual control through a wide craniotomy. Historically the targeting used an indirect location relatively to internal markers (anterior and posterior white commissures, ACPC). With the progress of MRI a direct location, based on the visualization of target, is now possible. It simplifies the stereotactic technique and parallel opens the field of analysis of relationships between function, electrophysiology and anatomy.

1. Description of purpose

The direct targeting method is still rare in functional neurosurgery because it implies a technical evolution with an MRI based analysis of brain anatomy. The implantation of deep brain stimulation (DBS) electrodes can be performed with this new approach if both anatomical structures (stereotactic targets) and surgical markers (used to calibrate the stereotactic frame or the surgical robot) are visible on stereotactic imaging.

We have developed this targeting for STN in its complex anatomical environment. The aim was to secure and to simplify the targeting as well as to provide a robust reproducibility. Preliminary clinical results have been already reported (ref.). This work focused on the subthalamic MRI mapping to evaluate its reliability, and parallel it throws light on the comprehensive anatomy and physiology of this region.

2. Methods

Data were prospectively collected during standard surgical procedures in 15 consecutive unselected parkinsonians operated on for bilateral implantation of DBS electrodes. Selection criteria and surgical environment followed the guidelines of the French Health Agency (ANAES 2000). The direct STN targeting used stereotactic (with the stereotactic frame and its location box in place) MRI slices (Siemens 1.5 Tesla machine). Coronal T2-weighted images (Cortex Attenuated Inversion Recovery sequence) led the determination of main anatomic structures with the help of classical anatomic books and in house 3D anatomy 4.7-Tesla MRI software (Fig.1). Clinical and electrophysiological data were collected peroperatively under local anaesthesia. This was done when seeking the best place for DBS according to the stimulation parameters, i.e. the current thresholds leading benefit and adverse effects. The stimulation parameters with their linked clinical effects (benefit on rigidity and on tremor; gaze, neurovegetative, sensitive and motor adverse effects) as well as the extra cellular recordings of neuron activity were noticed along trajectories, with respective steps of 1 mm and of 0.5 mm.

Relationships between electrophysiological and clinical data and MRI anatomy were studied by a side by side analysis (30 hemispheres). Statistics was performed with SAS (v8.02, USA): 1°) one way analysis of variance, completed by multiple comparison procedure computed using Tukey's method in case of overall significance, and Student t test for quantitative data; 2°) Pearson χ^2 and Fischer exact tests for qualitative data. A statistical significance was accepted for a p value below 0.05.

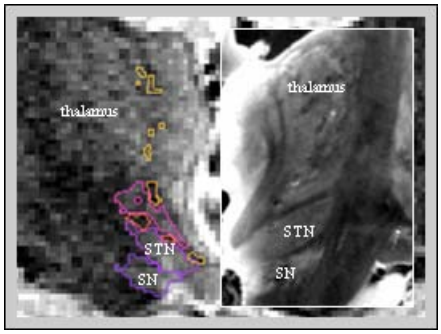

Figure 1: *Example of anatomic mapping on a T2 weighted coronal image (left) and the anatomical information of in house software (right): STN,*

3. Results

We found statistically significant relationships between subthalamic structures and stimulation data confirming the pertinence of the MRI anatomical study. The anterior dorso-lateral STN was the best candidate for DBS with at once a low current threshold leading benefit and a high current threshold leading adverse effects (Fig.2). Extra cellular neuronal activity was maximum in the anterior ventro-medial STN and the adjacent substantia nigra.

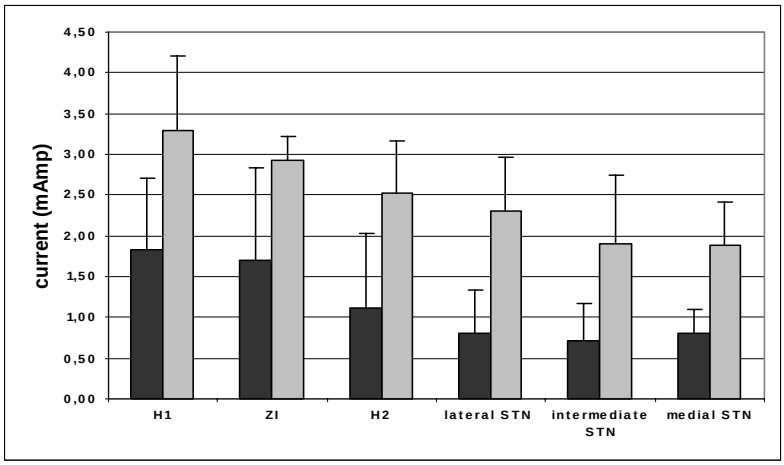

Figure 2: S*timulation parameters according to anatomical structures (Forel's fields, H1&H2, zona incerta, zi and STN subparts): mean value of current leading a benefit*

4. Breakthrough in stereotactic functional neurosurgery

Results show that in stereotactic conditions and with clinical MRI machine, dedicated sequences provide relevant anatomical information. In this way, it seems possible to map the subthalamic region with accurate details facilitating the direct stereotactic targeting for DBS. This new approach opens perspectives to analyze DBS effects as well as to study new stereotactic targets in functional neurosurgery.

5. Conclusions

Beyond the surgical spin-offs, in terms of time wining and of care improvement, the direct targeting based on MRI anatomical mapping offers the opportunity to revisit stereotactic functional surgery. It also gives prospects in the domain of invasive focal treatments of brain diseases

Ref.*: Caire et al. (2005*). Stimulation sous-thalamique dans la maladie de Parkinson sévère: Étude de la localisation des contacts effectifs. Neurochirurgie (in press). *Lemaire et al. (2001).* Deep brain stimulation in the subthalamic area for severe idiopathic parkinson's disease : location of plots in the peroperative phase and at the three month follow-up. Parkinson's & related disorders (abstract) 7, suppl, S80

Speaker: Mark Cohen, Ph.D.
Title: Professor of Psychiatry, Neurology, Radiology, Psychology and Biomedical Physics
Institution: UCLA School of Medicine
Time: 11: 00 – 11:20 AM
Topic & Abstract:

Integrative Methods in functional Neuroimaging

Functional MRI is a powerful means to identify brain regions involved in task processing for sensory, motoric and cognitive behaviors. Nevertheless, it has severe limitations in temporal resolution that constrain its use in the study of moment-to-moment processing. This talk will consider, primarily, the integration of multi-modality information from concurrent electrical recording to enhance both the temporal resolving power and the ability of fMRI to probe covert events that might not be expressed in directly observable behavior.

This talk will focus on extensions of functional MRI to probe the activity of the nervous system at higher spatial and temporal resolution by integrating multimodality information into the collection and analysis stream.

Co-Chair: Chi Zee, MD
Title: Professor of Radiology and Neurosurgery, Director of Neuradiology

Institution: USC-Keck School of Medicine

Time: 11: 20 – 11:40 AM

Topic & Abstract:

Clinical Application of Diffusion Tensor Imaging

In recent years, diffusion tensor imaging (DTI) has emerged as a powerful method for investigating white matter architecture in health and disease. Diffusion tensor imaging (DTI) is the more sophisticated form of DWI, which allows for the determination of directionality as well as the magnitude of water diffusion. This kind of imaging can estimates damage to nerve fibers that connect the area of the brain affected by a various disease entities such as stroke, brain tumor, head trauma, multiple sclerosis, epilepsy, Alzheimer's disease and Schizophrenia.

In patients with brain tumor, DTI can be used to show whether the white matter tract is infiltrated or displaced by the neoplasm. It can also reveal the extent of damage to the white matter tract caused by brain tumor. The information obtained from DTI can be used to guide surgical planning, and possibly to predict outcome.

In patients with head trauma, particularly those suffering from diffuse axonal injury (DAI), DTI can be used to demonstrate the extent of white matter injury due to head trauma. Studies are currently under way to correlate clinical findings with imaging findings on DTI and to evaluate the prognostic value of DTI in the evaluation of patients with head trauma and DAI.

DTI can demonstrate subtle changes in the white matter associated with diseases such as multiple sclerosis, epilepsy and Alzheimer's disease, as well as assessing diseases where the brain's wiring is abnormal, such as schizophrenia. Studies are currently under way to obtain new information in regard to these disease entities and hopefully DTI can be used to guide the treatment of these disease processes.

Speaker: Peter Conti, M.D.

Title: Associate Professor of Radiology, Clinical Pharmacy and Biomedical Engineering and Director of the USC Positron Imaging Science Center and Clinic

Institution: Keck School of Medicine

Time: 11: 40 – 12:00 AM

Topic & Abstract:

Molecular Imaging of Brain Tumors

Advances in biology have laid the groundwork for the development of molecular-based medicine—the identification and correction of molecular errors that underlie disease. This, coupled with rapid innovations in imaging and computing technology, has resulted in a new scientific discipline: "molecular imaging". Broadly defined, molecular imaging encompasses non-invasive visualization of the molecular processes of life in organisms ranging in complexity from individual cells to human beings. Molecular imaging appears destined to become the primary mechanism by which new discoveries are translated into clinical use and optimized for individual patients.

Molecular Imaging is a rapidly emerging discipline that unites investigators from the fields of cellular biology, molecular biology, bio-informatics, biochemistry, chemistry, combinatorial chemistry, physics, engineering, and numerous clinical areas including radiology, radiation therapy, medicine, surgery, neurology, cardiology and others. Imaging technologies currently employed include radionuclear [positron emission tomography (PET), single photon emission tomography (SPECT), autoradiography], magnetic resonance [spectroscopy (MRS) and smart contrast agents, as well as conventional anatomic imaging], x-ray computed tomography (CT) and optical imaging [in vivo fluorescence and bioluminescence, confocal fluorescence microscopy]. Some of the current applications of molecular imaging include non-invasive visualization and measurement of cell trafficking, tumor growth and spread in the absence or presence of treatment, expression of endogenous as well as exogenously implanted genes, pharmacokinetics and pharmacodynamics, enzyme activity, receptor density and protein-protein interactions.

In this presentation the focus will be on the development of tools and approaches for three current areas of investigation in molecular imaging of brain tumors: cell proliferation, gene therapy and angiogenesis. Non-catabolized radiotracers for imaging cell proliferation, namely C-11 and F-18 labeled 5-methly- 2'-fluoro arabinofuranosyluracil (FMAU) will be discussed in the context of animal studies and clinical trials. In the area of gene therapy, development of the radiolabeled analogues of the anti-virals ganciclovir and penciclovir, the latter currently being the gold standard for imaging gene expression with herpes simplex virus thymidine kinase (HSV-tk) reporter, will be presented. Finally novel ligands for imaging the avb3 integrin receptor within the cascade of the process of angiogenesis will be visited.

Speaker: Linda Liau, M.D., Ph.D.

Title: Associate Professor of Neurosurgery

Institution: UCLA School of Medicine

Time: 12: 00 – 12:20 AM

Topic & Abstract:

Image Guided Surgery and Intraoperative MRI

OBJECTIVE: To compare the extent of glioma resection using high-field strength (1.5-Tesla) intra-operative MRI (iMRI), low-field (0.2-Tesla) iMRI, and conventional frameless stereotactic neuronavigation without iMRI.

METHODS: 45 patients with supratentorial gliomas were divided into four groups: conventional operating room (OR) with standard frameless neuronavigation (n = 12); 0.2-T iMRI without neuronavigation (n = 13); 1.5-T iMRI with standard neuronavigation but no intra-operative re-registration (n = 10); and 1.5-T iMRI plus intra-operatively updated neuronavigation (n = 10). To validate the extent of surgical resection, 3-D volumetric analyses were performed on pre-operative versus early post-operative MR images.

RESULTS: The percent of resection using the conventional OR was 79 ± 24%, which was lower than that using 0.2T iMRI (91 ± 7%) and 1.5-T iMRI (92 ± 12%), although the differences were not statistically significant. When iMR-updated neuronavigation was added, the percent-resection was increased to 98 ± 2%, a value which was significantly better than that achieved in the conventional OR using standard neuronavigation alone ($p = 0.03$). Furthermore, residual post-operative tumor volumes were significantly and consistently lower using the 1.5-T iMRI with updated intra-operative neuronavigation (1.2 ± 1.5 cm^3) compared to those of gliomas resected in the conventional OR (13 ± 14 cm^3, $p = 0.009$).

CONCLUSION: The optimal utility of iMRI lies in its ability to be combined with updated frameless neuronavigation. This allows the neurosurgeon to proceed with greater safety and confidence during tumor resection. This study also suggests that similar results can be obtained using either a high-field iMRI or a low-field iMRI unit, provided that the intra-operative image quality is suitable for meaningful interpretation.

Luncheon Speaker: Andrea K. Scott, JD

Time: 1:30 – 1:50 PM

Special Topic: ETHICAL AND LEGAL PARAMETERS OF CENTRAL NERVOUS SYSTEM REPAIRSAL

The legal foundations of medical practice are based on the Hippocratic principal of APhysician, do no harm.@ In the near future, society will ask if central nervous system [ACNS@] repairs are qualitatively different from other medical procedures for restoring function. For the physician, there is no meaningful difference. For society, however, the issue is not limited to repairs and restoration of function. It includes the potential for enhancing the human brain. This raises the slippery slope argument that scientists will attempt to create a super-being.

Historically, self-serving politicians have used bad science to justify personal agendas and pork barrel projects. They have exploited public ignorance and misconceptions about complex medical research in order to manipulate and cut governmental funding for crucial growth areas of medical science. As technologies for brain mapping and restoration of lost function evolve, the need for informed societal dialog and public policy increases dramatically. We can divide many of the concerns about CNS repairs into four questions.

First, do we have sufficient understanding of the CNS to avoid unintended consequences caused by the repair mechanism and intervention? Second, which patients are appropriate for CNS repair? Third, in a world of shrinking medical resources, who will (or should) pay for these technologies, procedures and rehabilitation? And fourth, where do we draw the line between restoration of lost function and improvement over baseline function, and enhancement for its own sake?
If you, as scientists, do not anticipate the potential for public misunderstandings about CNS repairs and the likely subsequent outcry for governmental regulation, it may be imposed upon you.

Scientific session III:
Functional Brain Mapping

Chair: Manbir Singh, Ph.D.
Title: Professor of Radiology and Biomedical Engineering
Institute: University of Southern California

Time: 2:00 – 2:20 PM

Topic & Abstract:

Diffusion Tensor Imaging and Functional MRI in Brain Mapping

Knowledge of brain regions involved in articulation and the axonal network connecting these regions is critical to neurosurgical planning and navigation. Functional MRI detects regions activated during specific tasks and Diffusion Tensor Imaging (DTI) based Tractography detects axonal connections through white matter. However, there are technological challenges limiting the accuracy of both modalities. Functional MRI does not demarcate the actual site of neuronal activation, but instead, the entire local vasculature, including the micro and macro-vasculature is detected, and the challenge is to differentiate the micro-vasculature from the macro-vasculature. In tractography, the challenge is to quantify connectivity and resolve issues such as fiber-crossing within a voxel. The results of our work presented here suggest that it is possible to separate the micro from the macro-vasculature through a temporal tracking of the fMRI signal, connectivity can be quantified through normalized regions of interest (ROI) filtering, and fiber-crossing issues can be addressed by a novel Independent Component Analysis (ICA) based unmixing approach.

Co-Chair: Louis Lemieux , Ph.D.

Title; Professor of Physics Applied to Medical Imaging Department of Clinical and Experimental Epilepsy

Institution: Institute of Neurology, University College London

Time: 2:20 – 2:30 PM

Topic & Abstract:

EEG-correlated fMRI for Localization in Epilepsy

Abstract is not Available.

Speaker: SungWon Chung, Ph.D.

Institution: UCSFSchool of Medicine

Time: 2:30 – 2:50 PM

Topic & Abstract:

New Insight into the role of Superior Longitudinal Faciculus

Authors: SungWon Chung, Mitchel S. Berger, Jeffrey I. Berman, MariaLuisa Gorno-Tempini, Roland G. Henry

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Abstract

Introduction: DTI white matter tractography (WMT) is non-invasive tool to investigate white matter pathways, including superior longitudinal fasciculus (SLF), the role of which still elusive. Several reports demonstrated SLF using WMT, but exact location of SLF near the cortex has not been quantified. Based upon the notion that different part of frontal lobe serves different aspects of language, we sought to infer the role of SLF by measuring the location of SLF in the frontal lobe, using WMT and electrocortical stimulation (ECS).

Methods: 15 healthy subjects and 10 brain tumor patients were scanned for DTI, and patients underwent ECS as well to acquire speech arrest sites. WMT was performed and group probabilistic map of SLF was created for the quantitative localization. In healthy subjects this was done in atlas-based approach, by normalizing track mask into standard space, and in the tumor patients speech arrest sites served as the common reference point. Distribution of SLF in the frontal lobe was reported.

Results: In the healthy subjects, SLF near frontal lobe was found to be concentrated around inferior precentral sulcus, encompassing Brodmann's area 6 and 44. In the tumor patients, SLF was found to be distributed near the speech arrest sites.

Discussion: SLF was found to be distributed around inferior precentral sulcus and speech arrests within the frontal lobe. Since speech arrest sites are known to be frequently located near the inferior precentral sulcus, results from healthy and tumor subjects with different approach of analysis lead SLF to one anatomically and functionally defined region, articulation center. This

supports the notion that SLF constitutes the articulatory loop connecting posterior inferior frontal gyrus and posterior perisylvian region.

Preferred presentation type: oral presentation

Keywords: diffusion tensor imaging, electrocortical stimulation, superior longitudinal fasciculus, articulation, speech arrest

1. Description of Purpose
To Better understand the role of SLF in the language network by using diffusion tensor MRI tractography and intraoperative awake electrocortical stimulation

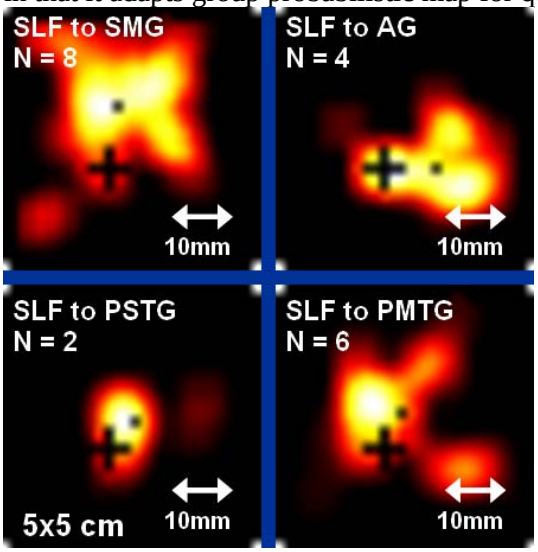
2. Methods
Group probabilistic map of SLF by track mask from multiple subjects using DTI tractography was combined with anatomic, atlas-based approach (using standard MNI space template) and functional approach, electrocortical stimulation mapping induced speech arrest sites to quantify the location of SLF in two complementary methods.

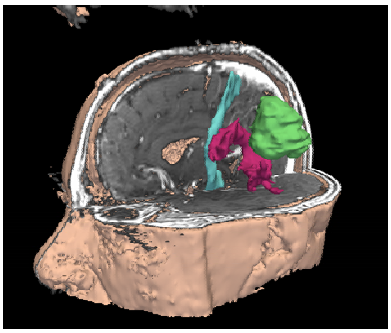
3. Results
Exact location of distribution of SLF in the frontal lobe was determined to be in the inferior precentral sulcus, including Brodmann's area 6 and 44, and also closely located to speech arrest sites.

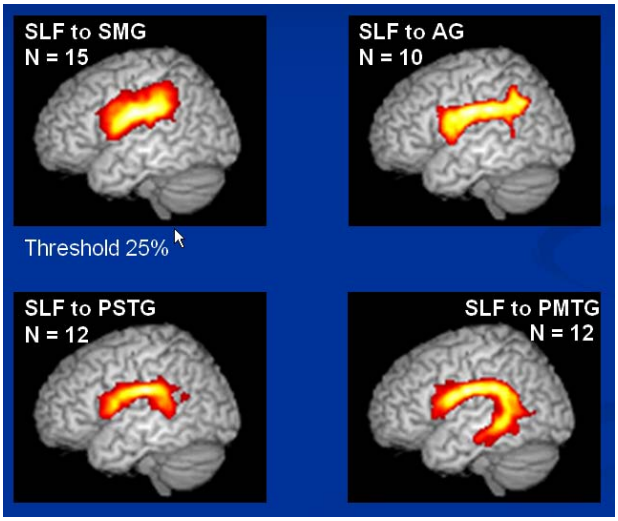
4. New of breakthrough work to be presented
Exact location of distribution of SLF in the frontal lobe was determined to be in the inferior precentral sulcus, including Brodmann's area 6 and 44, and also closely located to speech arrest sites.

5. Conclusions
SLF is anatomically linked to articulation center in the posterior inferior frontal gyrus, supporting the notion that SLF is part of articulatory loop.

6. Preliminary results of this work has been presented in the ISMRM, and this submission differ in that it adapts group probabilistic map for quantitative localization with more subjects.







Speaker: Jeffery Burman, Ph.D.
Institution: UCSF School of Medicine
Time: 2:50 – 3:10PM
Topic & Abstract:

Accuracy of Diffusion Tensor MRI Tractography Assessed with Subcortical Intraoperative Stimulation and Magnetic Source Imaging

Jeffrey I. Berman
Mitchel S. Berger
SungWon Chung
Srikantan S. Nagarajan
Roland G. Henry

Keywords: DTI Fiber Tracking, Brain Tumor, Intraoperative Stimulation, Surgical Navigation

Abstract:

Knowledge of the location of the pyramidal tract in relation to a brain tumor is important for deciding if resection is feasible and for maintaining a margin of safety between the resection cavity and functional pathways. If the descending motor pathway is damaged during brain surgery, the patient is likely to experience post-operative motor deficits. This study evaluates the accuracy and validity of a preoperative, non-invasive diffusion tensor MRI fiber tracking method to localize the motor tract in subcortical white matter. DTI fiber tracks were generated preoperatively using regions drawn based on anatomical landmarks. A mask of the resultant fiber tracks were overlaid on high resolution T1 and T2-weighted anatomical images and used for stereotactic surgical navigation. During surgical resection, subcortical stimulation of the motor pathway was performed within white matter using a bipolar stimulator. A total of 16 subcortical motor stimulations were stereotacically identified on 9 patients. The mean distance between the stimulation sites and the DTI fiber tracks was 8.7 ± 3.2 mm. The observed gap between the stimulation sites and DTI fiber tracks is expected because of electrical current penetration depth during bipolar stimulation. The precision of the DTI fiber tracking technique is affected by brain shift, stereotactic registration error, and DTI fiber tracking error. Juxtaposition of DTI fiber tracks with magnetic source imaging (MSI) sites was also observed. This study suggests the clinical validity of using DTI fiber tracking as a routine method of delineating the motor tract.

Purpose: Diffusion tensor imaging (DTI) fiber tracking of the pyramidal tract has been demonstrated to show connectivity between functionally mapped cortex and known anatomical landmarks. However, the accuracy and validity of fiber tracks' position within deep white matter structures has not been verified. Intraoperative subcortical stimulation is an invasive technique performed by neurosurgeons used during tumor resections to identify the location of the motor tract within white matter. Subcortical stimulation is the clinical gold standard and only functional method for identifying the pyramidal tract in deep white matter structures. In this study, fiber tracks constructed preoperatively are compared with the location of subcortical motor stimulations and magnetic source imaging (MSI) sites to evaluate the validity and accuracy of DTI fiber tracking of the human motor tract.

Methods: MR scans of 9 glioma patients were performed on a 1.5T GE Signa machine one day prior to surgical resection. DTI was performed with b=1000s/mm^2, TR/TE = 10000/100ms, slice thickness between 2 and 2.3 mm, no gap, voxel volume between 4.5 and 9 mm^3, 6 NEX, and six diffusion gradient directions. Magnetic source imaging (MSI) was performed on 7 of the patients to identify somatosensory corticies.

DTI fiber tracking of the pyramidal tract was performed presurgically by continuously following the primary eigenvector [1]. Fiber tracks were launched from the cerebral peduncle and targeted with regions drawn in the posterior limb of the internal capsule and the precentral gyrus. The DTI echo planar volume was registered to high-resolution FSE MR images with a 12-parameter model. Fiber tracks were overlaid on FSE images for use during surgery with the stereotactic navigation system (Medtronic, Broomfield, CO).

Direct electrical stimulation of subcortical white matter within the resection cavity was performed with a 5mm wide bipolar electrode to find points that elicited a motor response [2]. These points were stereotactically identified on the FSE MR images and screen saves from the navigation system were saved. The distance between the stimulation site and the closest border of the presurgical motor fiber tracks was measured.

Results and Discussion: 16 subcortical stimulation sites (4 upper extremity, 8 face or mouth, 3 lower extremity) were identified among the nine patients. The average distance between stimulation sites and DTI fiber tracks was 8.7 ± 3.2 mm. The distance measured is affected by

brain shift, the penetration of electrical stimulation, and variability in the location of fiber tracks. Brain decompression during resection can shift brain structures towards the electrodes and therefore give an artifactual offset to the fiber tracks. In addition, stimulation is known to penetrate brain tissue on the order of 5 to 10 mm. Since the resection is stopped when a motor tract is detected, the stimulation range sets a minimum distance between an observed stimulation site and fiber tracks. Figures 1 and 2 show the juxtaposition of subcortical stimulation sites, MSI sites, and DTI fiber tracking.

This work suggests the validity of the spatial distribution of DTI fiber tracks. DTI fiber tracks were constructed presurgically and matched the gold-standard for localizing the motor pathway within an acceptable margin of error. At UCSF, DTI fiber tracking of the motor system has become a routine presurgical exam for brain tumor patients undergoing intraoperative brain mapping.

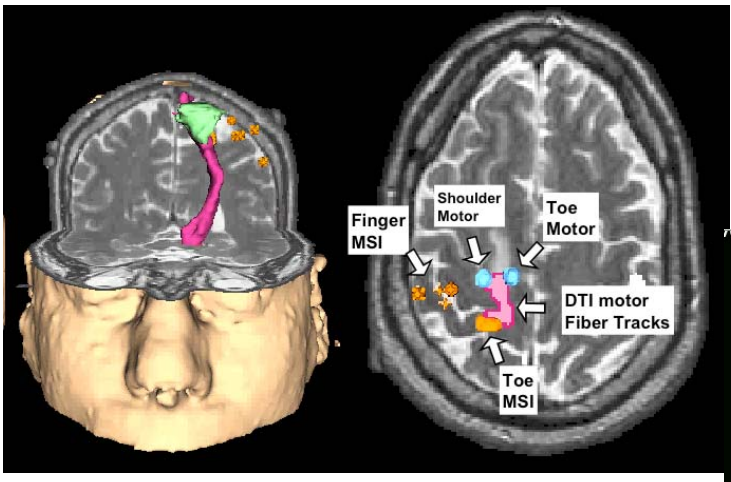


Figure 1: MSI sites (orange) and subcortical motor stimulations sites (blue) are projected onto axial slice with presurgical motor DTI fiber tracks (red). All sensory and motor sites are within 1cm of level shown. The four finger MSI sites are in the post central gyrus and lateral to the toe sensory MSI site. The motor fiber tracks and subcortical stimulations are in the precentral gyrus.

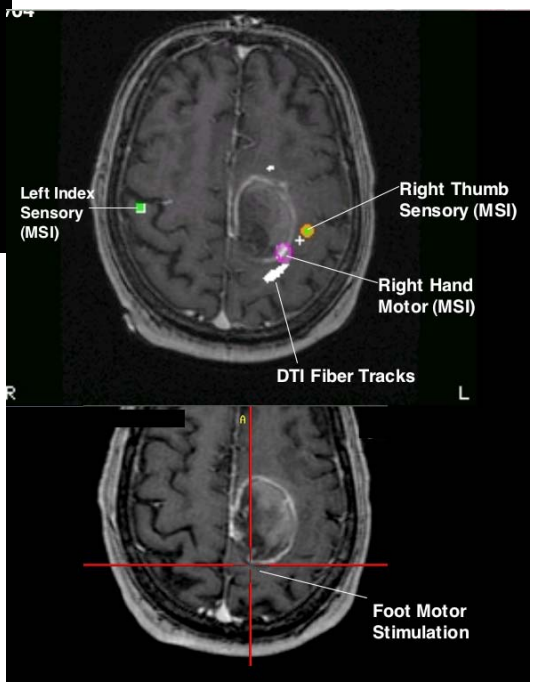


Figure 2: Illustrative case showing the compression of the motor and sensory tracts along the posterior border of the lesion. MSI thumb sensory (orange), MSI hand motor (purple), DTI fiber tracks (bright white), and foot motor stimulation (bottom, crosshairs) are shown.

References:

1) Mori, S., et al. Ann Neurol., 45: 265-269.

2) Berger MS, Ojemann GA. Intraoperative Monitoring Techniques in Neurosurgery. New York, McGraw-Hill, 1994, pp 113-127.

Funding from NIH/NCI CA100331

Speaker: Heather O'Leary, B.Sc., M.S.
Title: Researche Associate
Institute: Harvard Medical School
Time: 2:50 – 3:30PM
Topic & Abstract:

Design of Neuro-feedback Software Using Trial-Based Functional MRI on Motor Imagery

Heather M. O'Leary[1], Lawrence P. Panych[1], Jong-Hwan Lee[1], Nan-Kuei Chen[1], and Ferenc A. Jolesz[1], Seung-Schik Yoo [1&2&3]

1. Department of Radiology, Brigham and Women's Hospital, Harvard Medical School
2. Department of BioSystems, Korea Advanced Institute of Science and Technology
3. Neuroimaging Center, Gachon Medical School

Abstract:

Traditionally Functional magnetic resonance imaging (fMRI) has been used to detect cortical activation by measuring the contrast of oxygenated blood (BOLD). fMRI has recently been used to detect a sensory imagery task whereby the primary and secondary somatosensory areas are activated in the absence of external stimulus or muscle contractions. [Thompson et al. 2001; Yoo et al. 2001; Schurmann et al. 2002] Motor imagery tasks combined with trial based fMRI can be used to measure the changes in BOLD contrast and provide task performance feedback to a subject. To provide feedback to a patient Software must be developed that can operate in near real time fMRI protocol, utilize a reproducible method for quantifying the cortical activation, and present feedback to the patient.

We have implemented a trial based, 1 task per trial, and an event-related, multiple tasks per trial, protocol for near real time imaging in a 3T scanner. We further identify that BOLD contrast is the most reproducible method for quantifying activation from a recent study conducted using both a motor imagery task and an auditory task. Lastly, we develop a method for displaying neuro-feedback to a patient by calculating an activation mask from the trial based fMRI and measuring BOLD contrast for each TR in 3 TR increments. This software will soon be tested with subjects that have both practiced the motor imagery and auditory tasks and those who have not.
(ALSO FULL PAPER)

Keywords: neuro-feedback, fMRI, trial-based, event-related, reproducibility

Introduction:

Traditionally functional magnetic resonance imaging (fMRI) has been used to measure active regions of the brain by detecting and spatially mapping the contrast of oxygenated blood (BOLD). fMRI is used to detect a sensory imagery task whereby the primary and secondary somatosensory areas are activated in the absence of external stimulus or muscle contractions. [Thompson et al. 2001; Yoo et al. 2001; Schurmann et al. 2002] Motor imagery tasks combined with trial based fMRI is used to measure the changes in BOLD contrast and provide task performance feedback to a subject so that they may assess and enhance their performance during a scan session. In order to implement a system where Neuro-feedback can be provided to a patient the following components must be determined: a method for real time or near real time fMRI assessment, a reproducible method of quantifying the patient's performance on the task, and a method for providing information to the patient about their performance on the task.

Method:

Each subject is required to perform a motor imagery and an auditory task. The motor imagery task consisted of cueing the subject to imagine clenching their right hand for a 5 second interval. The auditory task consisted of a 900Hz tone amplitude modulated at 6Hz, range of 47.5dB +/- 30% sound pressure level (SPL), with a 5 second interval of an amplitude modulated tone at 6Hz, with a range of 72.5 dB SPL +/- 30%, and a frequency modulated tone at 6Hz, with a frequency range of 900Hz +/-12%. The regions of interest (ROI) that were examined were the contra lateral side of the precentral gyrus (motor imagery task) and bilateral Hescle's gyrus (auditory task). The fMRI signal is acquired to first determine the mask for activation using trial based fMRI and later to detect continuously the cortical activation as the subject attempts to enhance their performance. Trial based fMRI is a paradigm where the subject is instructed to perform 1 task over a brief interval (5 seconds) while the functional scan is acquired. An echo planar image (EPI) sequence (24cm field of view, 5mm thickness with a 1 mm gap, 13 slices, flip angle of 30, and TE/TR of 40/1000msec) was acquired from a 3T (GE medical systems) scanner. For the neuro-feedback task, the same EPI sequence is repeated for approximately 2 minutes. The subject is cued to begin the task after 20seconds and repeats the task several times during the scan session. An ftp script is used to transfer each new EPI file as they are written to a laptop used for processing the data. Due to the limitations of data transfer the EPI data must be processed in near real time (1 file contains 3 volumes). Activation is measured using software written in MATLAB that uses the mask generated from 3 previous trial based scans and display with MR compatible goggles.

Results:

Characterization of variability of cortical activation in trial based fMRI is important in the implementation of neural feedback because the BOLD contrast is calculated multiple times during a single continuous [deCharms et al 2004, Weiskopf et al 2004] or segmented [Yoo et al.] session. We determined the reproducibility of cortical activation by measuring the volume of activation and the BOLD contrast of a motor imagery task and an auditory task in 10 (8 male) healthy 19-49 year old (mean 27.9 +/-8.9), 9 right-handed subjects. An EPI sequence was acquired from a 3T GE scanner for 10 trials per subject. Cross correlation was used to identify active pixels within each ROI for thresholds ranging from p=.01 to p=.0001. Reproducibility is defined as the percent standard deviation (SD) of the mean intersession activation divided by the mean activation. Figure 1 shows the percent SD versus the log scale of 5 threshold conditions for both the motor imagery and auditory tasks for "A" (the volume of activation) and "B" (the BOLD contrast). It is demonstrated by the plots that the BOLD contrast has a lower percent SD than the volume of activation and, therefore, is the best method for quantifying trial-based fMRI cortical activation. In addition, no linear trend was found in the percent standard deviation of the BOLD contrast measurement for both the motor imagery and the auditory task, indicating that BOLD contrast is independent of threshold conditions.

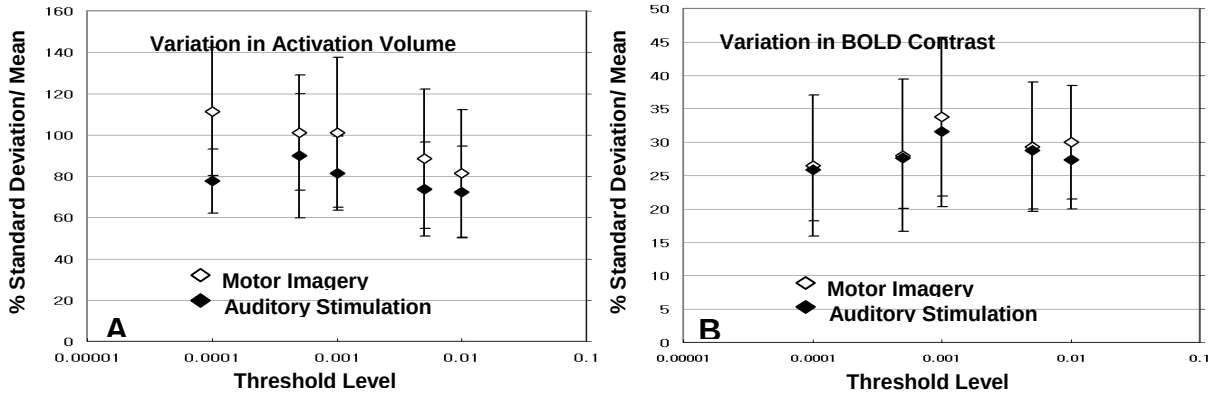


Figure 1. The percent variation of reproducibility indicator (the stand deviation with respect to the mean inter session value out of 10 sessions) averaged from 10 subjects in terms of the (A) activation volume and (B) BOLD contrast, plotted for the 5 threshold conditions (in log scale in x-axis). White diamonds indicate the motor imagery task, and the black diamonds indicate the auditory task. Note that the measurement was independent from the range of threshold conditions used and almost identical for two different tasks when the BOLD contrast was used for the parameter.

Conclusion:

The study of reproducibility in trial based fMRI has shown that motor imagery can be detected for brief task intervals and that BOLD contrast is a more reliable method of quantifying cortical

activation. In lieu of this study we have developed a neuro-feedback software design. The presentation of neuro-feedback will be achieved by first using trial based fMRI to extract the active pixel mask from within the ROI, acquiring and processing the EPI in real-time, and displaying a plot of the mean BOLD contrast versus time to the subject through MR compatible goggles. This software will soon be tested with subjects that have practiced the task (1 day per week for 2 weeks) and subjects for whom the stimulus is novel.

Submission Information:

This research is novel and has not been submitted for publication or presentation elsewhere.

References:

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Scientific session IV:
Brain Mapping and Intra-operative Surgical Planning using Endoscopy

Chair: John Frazee, MD
Title: Professor of Neurosurgery and Director of Neuroendoscopy at UCLA
Institution: UCLA School of Medicine
Time: 4:00 –4:20 PM
Topic & Abstract:

Advance Neuroendoscopy: Present and Future

The use of the endoscope for neurosurgical procedures was limited to rare cases until the late 1980's. Activity grew in short bursts with the endoscope being used primarily for intraventricular work including tumor biopsy and hydrocephalus. The failure to advance was related to poor equipment, often borrowed from other subspecialties, a very steep learning curve, which discouraged most neurosurgeons, and the lack of corporate support. In the last few years all of this has changed. New neuroendoscopes, with a variety of tools, including bipolar, have been built. Special anatomically accurate teaching models have been created. Advanced courses in neuroendoscopy have been offered. Importantly, the scope of application has been broadened to include not only surgery within the ventricular system, but also within the brain parenchyma and along the skull base. The endoscope has begun to replace the microscope in some areas such as transnasal pituitary surgery. With the further development of a user-friendly endoscope, it is hoped that most neurosurgeons can readily the endoscope to their practice. Selected videos for endoscopic and endoscopically assisted surgery will be shown including hematoma evacuation,

arachnoid cyst fenestration, collicular plate tumor biopsy, and aneurysm surgery. Advanced instrumentation will be demonstrated.

Co-Chair: Warren Grundfest, MD
Title: Professor of Surgery and Biomedical Engineering
Institution: UCLA, President IBMISPS (2006-2007) and Board member
Time: (4:20 – 4:40 PM)
Topic & Abstract:
The Trans-Blood Vision Imaging System

Neuroendoscopy can be performed using rigid or flexible endoscopes, but bleeding causes image distortion followed by complete loss of the image. The inability to see through blood limits the efficacy of the procedure and increases the risk of unintended injury. A new imaging system that allows imaging through blood has been developed for application in a cardiovascular system. The system uses infrared laser light, infrared imaging and illumination fibers, and a special CCD camera sensitive to the IR light to obtain images via a 7 French flexible catheter. The images are black and white, but can be colorized for greater clarity.

Scattering theory predicts that when the wavelength of light is longer than the particle size, it should be possible to see through blood. This theory has been validated in invitro experiments and animal models. Initial clinical use demonstrated the ability to see through two cm of blood in the right atrium during pace maker lead placement procedures in two patients. The black and white images show anatomic details including the ostium of the coronary sinus and valve leaflets. In solutions with less hematocrit, it is possible to image for greater distances. This system may have unique applications for intracranial imaging permitting greater use of neuroendoscopy for minimally invasive surgical procedures.

Speaker: Marvin Bergesnieder, M.D.
Title: Associate Professor of Neurosurgery Co-Director of Neuroendoscopy at UCLA
Institution: UCLA School of Medicine
Time: 4:40 – 5:00 PM
Topic & Abstract:
Two-Port Endoscopic Microsurgical Excision of Colloid Cysts

Abstract is not Available.

Speaker: Tien T Nguyen, M.D.
Title: Assistant Professor of Neurosurgery
Institution: UCLA School of Medicine
Time: 5:00 – 5:20 PM

Topic & Abstract:
Intra-operative planning for Endoscopic Mmanagement of hydrocephalus

Neuroendoscopy is commonly performed by the neurosurgeon for the management of hydrocephalus. The endoscope is ideally used during third ventriculocisternostomy, aqueductoplasty, septum pellucidotomy, and fenestration of loculated ventricles. Brain imaging and operative planning before and during these surgeries are necessary to determine the appropriate surgery for selected patients and to minimize complications. An MRI obtained during work-up can differentiate communicating from non-communicating hydrocephalus. Addition of constructive interference steady state (CISS) and cine phase-contrast protocols during MR

imaging may detect a site of obstruction of cerebrospinal fluid (CSF) flow not visible with routine MRI. However, a regular MRI is still crucial in outlining the patient's ventricular anatomy and identifying vital brain and vascular structures adjacent to the surgical tract and target. Combining the MRI with a navigation system during surgery can thus help plan an approach to the target that would spare eloquent brain and large blood vessels and require minimal pivoting of the scope. Pre-operative and intra-operative planning with image guidance for endoscopic surgery for hydrocephalus can aid the surgeon in restoring the patient's physiological CSF flow and reduce procedure-related morbidity.

Speaker: David A. Feinberg, M.D., Ph.D.
Title: President and CEO. Advance MRI Technology. LLC, Adjunct Professor of Radiology and Physics
Institution: Washington University and Mallinckodt Institute, St. Louis
Time: 5:20 – 5:40 PM
Topic & Abstract: Dynamic MR Angiography and Blood Flow measurements in Arteriovenous Malformations, cerebral aneurysms and Atherosclerotic disease.

Introduction
MRI quantitative blood flow measurements can be made using basically one of two techniques. The 'time of flight' (TOF) technique tracks the position of blood movement. The phase map or often called 'phase contrast' technique measures the signal phase shifts induced with specific bipolar magnetic gradient pulses which measure the velocity vector components of motion. Presented here are the development of dynamic MR flow techniques specifically to study cerebrovascular diseases of AVM, aneurysm and stroke. A variant of TOF techniques is arterial spin labeling (ASL) techniques which tracks movement of blood into tissue, analogous to a tracer to obtain perfusion measurements in the brain.

Methods
A dynamic MRA technique was developed. The inflowing blood is labeled by inversion of its longitudinal magnetization followed by an image acquisition with a segmented FLASH sequence in a downstream position of interest. By repeating the image acquisition with different inversion times (TI) between blood tagging and image acquisition, the dynamics of blood arrival time in the arterial tree can be visualized and quantified, with parameters consistent with mean transit time (MTT). A dynamic MRA method had temporal resolution of 35ms, frame rate 28 images/second useful to resolve flow dynamics in the cerebral vessels including the Circle of Willis with no injection of contrast agent. The spatial resolution is 0.9 x 0.9 mm^2 with a slab thickness of 50mm.

The MR velocity phase imaging technique was modified in a protocol to image cerebral aneurysms. Cardiac gated sequences created cine movies of quantitative velocity vector components, 30 frames per second. The 3 velocity vector maps with tensor analysis produced maps of the aneurysm wall shear stress.

To obtain 3D perfusion maps of the brain, a single shot 3D GRASE sequence was combined with pulsed ASL technique. The sequence had maximum resolution of 6 seconds to acquire labeled and non labeled data sets for background supression. Signal averaging, N=10, was used to increase SNR for a total scan time of 1 minute.

Results
Flow dynamics in 10 patients with atherosclerotic disease were investigated.and showed alterations in Circle of Willis flow with delayed flow in presence of 'non significant' stenosis. Quantitative velocity measurements were made in 9 patients with cerebral aneurysms and showed vortices, points of flow jet impact on aneurysm walls and the wall shear. The perfusion measurements made in 30 patients show reliable quantitative brain perfusion in clinically

accessible scan times without the injection of contrast agents. More recent work with ASL 3D GRASE is useful for functional MRI with direct measure regional blood perfusion rather than by the BOLD venous response.

Discussion / Conclusion

In comparison to conventional x-ray DSA, there is comparative temporal resolution in the dynamic MRA without increased radiation exposure as in x-ray DSA. The quantitive measures of blood flow in AVM feeding arteries, nidus and draining veins offer new approaches to studying and differentiating the AVM pathology for risk of hemorrhage or stability. The velocity phase maps of cerebral aneurysms allows for measurement of kinetic energy and wall shear, which may be determinants of aneurysm growth or rupture. In conclusion, the new ability to obtain 3D maps of perfusion, blood flow in altered hemodynamics and hemodynamic parameters in aneurysms may be useful for surgical planning and monitoring therapeutic responses.

Second Day: Nov. 18th

Scientific Session V:
Stereotactic and Radiosurgery Planning:

Chair: Peter Gruen, M.D.
Title: Interim Chief Medical Officer (CMO) and Associate Dean LAC+USC
Institution: USC-Keck School of Medicine
Topic and Abstract:
No talk was presented by Dr. Gruen in this meeting. He was ONLY Chairing the session.

Co-chair: Farzad Massoudi, MD
Title: Associate Clinical Professor
Institution: UCLA, Massoudi Medical Group President of IBMISPS (2007-2008); IBMISPS Board Member
Time: *8:20 - 8:40 AM*
Topic and Abstract:

Farzad Massoudi, M.D., Stafford G. Chenery, Ph.D., Joel Cherlow, M.D., Steve Damore, M.D., Hazem H. Chehabi, M.D.
Newport Diagnostic Center, Newport Beach, CA

Introduction: CyberKnife radiosurgery has increasingly been recognized as an effective treatment for intractable trigeminal neuralgia. At Newport Diagnostic Center we performed the first Cyberknife treatment of trigeminal neuralgia in the world in 1999 and have since treated patients on a regular basis

Materials and methods: 29 patients with idiopathic trigeminal neuralgia were treated between 1999 and 2004 with a minimum of 6 months and a median of 18 months of clinical follow up after single fraction CyberKnife radiosurgical treatments. Single isocenter dose planning was used in all cases in which 5 mm collimator was utilized to deliver 8000 cGy to the root entry zone of the trigeminal nerve typically located within the intracisternal segment. High resolution 2mm thin cut brain MRI and CT Scans were obtained in each case. CT/MRI fusion was performed in all cases and the trigeminal nerve was identified using T2 weighted images. In 25 patients a blood

vessel coming into contact with the nerve was radiographically identified.Pre treatment phantom testing in every patient demonstrated accuracy of 0.9mm to 1.2mm. The average length of the treatment was 90 minutes.

Results: 17 patients (59%) had complete pain resolution and discontinued the use of their medications. 5 patients (17%) had significant pain reduction while continuing their medications. 3 patients (10%) had no change in the level of their pain and 1 patient experienced worsening of the pain. 9 patients reported significant post treatment facial numbness (31%) in 4 of whom the numbness was permanent. 2 of these 4 patients had bothersome numbness which was classified as anesthesia dolorosa (6%). The effectiveness of the treatment was noted between two weeks and five months after the treatment.

Discussion: In our single center 5 year experience with CyberKnife treatment of trigeminal neuralgia we have noted an overall 76% successful clinical outcomes with 31% rate of post radiosurgical numbness that in approximately 50% of the time is permanent. So far CyberKnife radiosugery appears to be a safe and effective method of treatment for trigeminal neuralgia.

Speaker: Antonio A. F. De Salles, M.D., Ph.D.
Title: Professor of Neurosurgery and Head of Stereotactic Radiosurgery
Institution: UCLASchool of Medicine
Time: *(8:40 - 9:00 AM)*
Topic & Abstract:
Novalis: Sparing Functional Brain

Antonio AF De Salles, MD, PhD; Alessandra Gorgulho, MD; Paul Medin, PhD; Nzhyde Agazarian, PhD; Timothy Solberg, Ph.D.; Michael Selch, MD

INTRODUCTION:
Functional changes in the central nervous system (CNS) are possible via destruction of pathways, nuclei or modification of cellular function. Precise, fast and homogeneous dose delivery becomes important in modern Functional Radiosurgery.

METHODS:
From December 1997 to April 2005 several approaches to Functional Radiosurgery were tested using the Novalis. Animal experimentation conducted for Parkinson's disease, Epilepsy and Chronic Pain supported the clinical use of Novalis in Trigeminal Neuralgia (176 patients), Cluster Headache (4 patients), Essential Tremor (3 patients), Chronic Pain (3 patients) and Epilepsy (5 patients). Homogeneous plans using the shaped-beam technique were developed to completely envelope mesial temporal structures related to Temporal Lobe Epilepsy.

RESULTS:
Modification of cell function was observed electrophysiologically and histologically in animal models for epilepsy and Parkinson's disease. Obliteration of pathways and nuclei were observed when targeting the spinal dorsal root ganglion, the root entry zone of the trigeminal nerve, the thalamus, the subthalamic nucleus. Functional changes related pain improvement was observed in patients with cluster headache by observing symptomatic relief. Homogeneous plans to the level of 10% from center to periphery were observed in planning for mesial temporal lobe structures modification.

CONCLUSIONS:
This experience shows that the Novalis technology is precise and capable of delivering high doses (150Gy) for tissue ablation, as well as low doses (15 Gy) tightly conformally and homogeneously for functional modification without radiation necrosis.

Speaker: Stafford Chenery, Ph.D.
Title: Physicist
Institution: Newport Diagnostic Center, Inc.
Time: (9:00 - 9:20 AM)

Topic & Abstract:
Image Manipulation and Isodose Planning Using the CyberKnife

The CyberKnife is an image guided robotic system designed to perform stereotactic radiosurgery for targets anywhere in the body. The system at Newport Diagnostic Center, the first commercial unit, was installed in 1996.
Sites treated since installation include intracranial and extracranial CNS, osseous sites from base of skull to spine, and paraspinal soft tissue. The Accuray treatment planning system was used to plan all cases. A strictly clinical approach is used in the planning process. Brain mapping is used in the determination of target and critical structures through the routine use of fused MRI and CT data. +/- 10% or better homogeneity of dose in the target is stipulated. The dose to critical structures is controlled using exact or volume dependent criteria. Multiple collimator sizes are used to control penumbra in critical structures adjacent to target. Dose per beam is limited to avoid hot spots in normal tissue in general. Dose to defined constraint points in the patient is limited in order to refine competing isodose plans. Actually treated clinical examples illustrating each of the above features are discussed.Keywords: image guided robotic radiosurgery, MRI/CT fusion, isodose planning

Speaker: Alessandra Gorgulho, M.D.
Institution: Neurosurgery Fellow at UCLA
Time: 9:20 - 9:40 AM

Topic & Abstract:
AVM Radiosurgery and Brain Mapping

Introduction: AVMs in eloquent areas and/or large in size are very challenging for all treatment modalities. When the AVM is suitable for surgery, careful preoperative planning and special intraoperative monitoring (brain mapping for instance) are necessary tools to provide safe resection. In case where lesions are not straight approachable by surgery, the development of new techniques and approaches in Radiosurgery (SRS) may allow broader indication of SRS for complex AVMs, which may or may not be followed by other treatment modalities.

Materials and Methods: From 1999 to 2002, 241 patients were treated with radiosurgery at UCLA. Ninety four patients submitted to 123 radiosurgery procedures were evaluated. The mean age was 35.4 years, 53 were female. Fifty two patients had embolization prior to radiosurgery and 11 had attempted surgical resection. The mean pre-radiation volume was 12.6 cc for the group submitted to embolization (SRS-E) and 10.8 cc for those treated with SRS alone (SRS-A). Thirty patients required repeated SRS. The mean peripheral dose was 15 Gy to the mean 86% prescribed isodoseline. Mean follow-up for SRS-E group was 50.4 months and 40 months for SRS-A.

Results: Overall obliteration rate was 46.8% (44 patients). The Spetzler-Martin classification, although created to predict surgical outcomes, also predicted radiation induced obliteration according to grade. The peripheral dose significantly decreased as AVMs became more sizable ($p<0.0001$). Therefore, obliteration rate decreased as volume increased. The minimum peripheral dose of 15 Gy was significantly correlated to obliteration ($p<0.023$, OR=2.74). The obliteration rate was better with Shaped Beam Radiosurgery than with the dedicated LINAC device, however not significantly better ($p=0.69$). Permanent neurological deficits rate was 0.84% per procedure in the SRS-A group and 1.68% for SRS-E. No permanent neurological deficit was noticed with Shaped Beam SRS, which allows a better conformity and homogeneity in comparison to the previous technique. Annual bleeding rate post-SRS was 0.74%.

Conclusions: As new techniques emerge and improve, some complexes AVMs not even amenable to treatment in the past may become treatable. Combination of multiple modalities with the use of the most sophisticated tools is necessary to make treatment offer under acceptable risk of complication.

Speaker: Reinhard Schulte, M.D.
Title: Assistant Professor of Radiation Medicine
Institution: Loma Linda University, School of Medicine
Time: 11: 30 – 11:50 AM

Topic & Abstract:

A System for Functional Proton Radiosurgery

Reinhard W. Schulte[1], Richard P. Levy[1], Tom S. Lee[2], Mahesh Neupane[2], Dominik Slusarczyk[3], Keith E. Schubert[2], and Jerry D. Slater[1]

1 Department of Radiation Medicine, Loma Linda University Medical Center, Loma Linda, CA, USA
2 Department of Computer Science, California State University, San Bernardino, CA, USA
3 Harvey Mudd College, Claremont, CA, USA

High-energy proton beams (250 MeV) have exquisitely sharp lateral penumbra with minimal widening as the beam penetrates the patient. Therefore, they are ideal for functional radiosurgery procedures such as pallidotomies and thalamotomies. Before functional proton radiosurgery can be implemented clinically, two technical challenges have to be overcome. First, guiding a narrow proton beam with a proton gantry that weighs about 90 tons to a target with submillimeter precision requires a sophisticated alignment verification system. Second, targeting the anatomical lesion location with an MRI-based fiducial system requires correction of gradient nonlinearity distortions inherent in the scanner images. Modern MR scanners are particularly prone to such distortions due to wider bores and stronger gradient fields. We are developing technical solutions to both problems that will be presented in this talk.

The alignment verification system utilizes three high-resolution CCD cameras (Vicon Motion Systems, Inc., Oxford, UK) in an equilateral triangular configuration, which are focused on a patient-based marker system (caddy), attached to the stereotactic halo, and a proton-beam-based marker system (cross) attached to the proton beam delivery cone. The gradient nonlinearity correction is based on a high-resolution 3D-mpr sequence scan of a cube phantom centered on the gradient isocenter of the MR scanner. Using a least-square fitting procedure correction parameters are found that convert the geometrically warped planes of the cube into the ideal

planes. The correction functions can then be applied to other scans. The mathematical method of this approach has been developed and results of its performance will be presented.

Scientific Session XIII:
Bio-photonics & Advance Devices

Chair: Warren Grundfest, MD
Title: Professor of Surgery and President of IBMISPS (2006-2007)
Institution: UCLA-School of Medicine and IBMISPS
Time: 9:10 - 9:30 AM
Topic and Abstract:

Biophotonics Technologies for Assessment of Cerebral Chemical Composition

Recent advances in optical coherence tomography (OCT), fluorescence imaging and hyperspectral imaging allow *invivo* study of brain structure and function. OCT permits imaging through 2-3 millimeters of tissue with resolution of 3-5 microns using near infrared wavelength. Fluorescence imaging using near UV excitation can identify ischemic cells and molecular markers. Hyperspectrual imaging has the potential to extract oxygenation status from the tissues. As these technologies evolve the ability to correlate optical signals with disease state will improve. Several additional optical techniques can be employed in neuroimaging. Lifetime fluorescence imaging uses sub-nanosecond UV laser light pulses to generate life time maps of tissue. These maps can be correlated with the chemical structure of the tissue.

New instrumentation for the lifetime imaging has been developed, which allows integration with endoscopic systems. Two-photon excitation may permit imaging through 5 millimeters of tissue extending the reach of optical technologies. These technologies should improve capabilities for the interoperatiove Diagnosis and procedure guidance.

Co-Chair: Neal Prakash,M.D.
Title: Associate Professor of Neurology
Institution: UCLA-School of Medicine
Time: (9:30 - 9:50 AM)

Topic & Abstract:
Advances in intraoperative brain mapping using optical imaging of intrinsic signals

Neal Prakash[1,2], Susan Bookheimer, Nader Pouratian[1], Sameer A. Sheth[1], Neil A. Martin[3], Arthur W. Toga[1,2]

1Laboratory of Neuro Imaging, Department of Neurology, David Geffen School of Medicine at UCLA, 710 Westwood Plaza Room 4238, Los Angeles, CA 90095
2Department of Bioengineering, Biomedical Engineering IDP, UCLA, Los Angeles CA 90095
3Division of Neurosurgery, Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, CA 90095
4Departments of [2]Psychiatry, Brain Research Institute, Interdepartmental Neuroscience Program, and Brain Mapping Center, UCLA, Los Angeles, CA 90095

EEG, functional MRI, and PET are functional brain imaging techniques have been used to study human cortical organization. However, these techniques have spatial resolution limited to at best, millimeters and are difficult to acquire intraoperatively. Optical imaging of intrinsic signals (OIS) is an emerging technique that offers perhaps the best combination of spatial coverage, resolution and speed for mapping the functional topography of human cortex. Advances in optical imaging

technology and methodology have made human OIS easier to implement and more accessible, including improvements in detector characteristics and the development of sophisticated algorithms for reducing motion artifact. Moreover, these advances have helped enhance our understanding of the functional organization of the human brain. Other advances include newly developed analyses for interpreting and validating optical signals, including refined signal analysis techniques and multimodality comparisons. Combined, these advances have enabled the study of not only primary sensory and motor cortices, but also higher cognitive processes such as language production and comprehension. Continued improvement and implementation of this technique promises to shed new light on the functional organization of human cortex.

Speaker: Changhuei Yang, Ph.D.
Title: Assistant professor of Electrical Engineering and Bioengineering
Institution: California Institute of Technology (Caltech)
Time: (9:50 - 10:10 AM)
Topic & Abstract:
Forward Imaging Optical Coherence Tomography Imaging Probe

Forward Imaging Optical Coherence Tomography Imaging Probe
Changhuei Yang (chyang@caltech.edu)
California Institute of Technology

We report a novel forward-imaging optical coherence tomography (OCT) needle probe - Paired Angle Rotation Scanning OCT (PARS-OCT) probe. The probe uses two rotating angled GRIN lenses to scan the output OCT probe beam over a wide angular arc (~28 degrees)and a reasonable depth (~ 3-4 mm) of the region forward of the probe. The probe's novel scanning method represents a very important technical advancement that will enable the construction of very compact needle probes. We have already demonstrated that a PARS-OCT probe prototype is capable of collecting OCT images of the forward cone region ahead of the probe tip. Amongst other advantages, this probe design is readily amenable to miniaturization and is capable of a variety of scan modes, including volumetric scans. The availability of a low cost, forward imaging needle probe can greatly improve the accuracy and utility of most needle surgical procedures, as well as anesthesiology procedures. Such probes may be used independently or in complement with existing image guidance systems, such as x-ray or ultrasound imaging.

Speaker: Steven Smith, Ph.D.
Institution: Xenogen Corporation
Time: 10:10 – 10:30 AM
Topic & Abstract:

Bioluminescent Imaging in Transgenic Mouse Models of Neurological Damage and Disease
Key words: GFAP, bioluminescent imaging, neuronal damage, bacterial meningitis

Introduction: Bioluminescent *in vivo* imaging is a tool that can be used to evaluate tissue damage, inflammation and the efficacy of drug treatment. We have generated a suite of transgenic (tg) mouse models containing the luciferase (*luc*) reporter driven by promoters of genes activated due to tissue damage and disease. The tg reporter constructs include promoters from GFAP, POMC, iNOS, VEGFR2, SAA1, NFκB-response elements, COX2, and iκB. These mouse models have been employed in the study of neuro-inflammatory disease, sepsis, and wound healing, as well as tumor onset and response to therapy. **Methods:** These studies examined the temporal and spatial inflammatory response and *luc* expression following bacterial infection in the CNS, following administration of MPTP, kainic acid and pro-inflammatory agents. **Results:** The *in*

vivo induction of the *luc* reporter following neuronal damage correlates with endogenous gene and *luc* transgene mRNA levels as well as tissue damage. **Conclusion:** These light producing transgenic animal (LPTA) models can be used for assaying inflammatory response, neuronal damage, and disease progression *in vivo* in real time. Using multiple LPTA models may elucidate a drug response pathway, location of tissue damage or identify sites of infection. **Discussion:** New instrumentation developed by Xenogen provides improved anatomical assessment of the tissues involved in the inflammatory response. The bioluminescent *luc* reporter or fluorescent reporter tags combined with Xenogen's IVIS® Imaging System 3-D imaging capabilities calculates the 3-dimensional location of the luminescent source *in vivo*.

Scientific Session VII
New Horizons in Medicine
Informatics, Robotics and fMRI

Chair: Stephan G. Erberich, Ph.D.
Title: Director of Functional Imaging Center at USC; Associate Professor of Radiology CHLA-USC; IBMISPS Board member
Institution: USC-CHLA
Time: 10:30 – 10:5 0 AM
Topic and Abstract:

Grid-Based fMRI Processing Service for Clinical and Neuroscience Brain Mapping

Functional Magnetic Resonance Imaging (fMRI) has been widely adopted as a non invasive method to located brain activation in clinical research. However fMRI remains to be a challenge in the clinical setup because sophisticated knowledge and standards required for paradigm development and post-processing are missing. Here we introduce the concept of a Grid based virtual functional Imaging Laboratory (Grid funcLAB) for large-scale routine clinical fMRI which provides standardized fMRI task processing as a Grid service. Remote sites, hospitals or practices, without local fMRI processing capabilities, can join the fMRI Grid and securely submit images for processing over the Internet using state-of-the-art Grid technology. We conclude that Grid based fMRI services are an ideal solution to connect image providers which lack fMRI processing capabilities together with processing providers, fMRI expert centers. Such a concept may be the technical solution to overcome the current hesitation for clinical use of fMRI, caused by the technical burden and large variability in results due to missing standardized processing.

Purpose:
Functional Magnetic Resonance Imaging (fMRI) has been widely adopted as a non invasive method to located brain activation in clinical research. Recent improvements in MR technology make functional imaging now available at the clinical level. However fMRI remains to be a challenge in the clinical setup because sophisticated knowledge and standards required for paradigm development and post-processing are missing. Here we introduce the concept of a Grid based virtual functional Imaging Laboratory (Grid funcLAB) for large-scale routine clinical fMRI which provides standardized fMRI task processing as a Grid service. Remote sites, hospitals or practices, without local fMRI processing capabilities, can join the fMRI Grid and securely submit images for processing over the Internet using state-of-the-art Grid technology. The resulting brain activation maps become available on the Grid in minutes after submission.

Methods:
We have developed a Grid service for automatic fMRI processing using the Globus Toolkit, a standard grid technology widely adopted in academia and industry. The current version 4 (GT4)

has been used in order to follow the Open Grid Service Architecture (OGSA) design – the standard directive in Grid computing. Key components provided by GT4 are flexible authentication and authorization mechanism based on X.509 certificates with delegation, distributed data processing, and remote data storage. DICOM fMRI images are send from the local MRI or PACS to a DICOM Retrieve Grid Interface Service (DRGIS). DRGIS compresses the images and notifies a Meta Catalog Service (MCS) about the image identification and exam parameters of each series. The MCS compares the description of the series with its fMRI reference library of know paradigms. Series are then marks as unprocessed fMRI and MCS invokes a Data Replication Service (DRS) which replicates the local images into the Grid image repository. The funcLAB Grid Service (FGS) queries the MCS for new images and retrieves unprocessed series from the DRS and an XML schema of the processing parameters from the MCS in the order of arrival. FGS starts the remote processing according to the XML schema and returns a PDF-file to the DRS and a reference to the MCS. The user can query the MCS for processed fMRI cases by patient id, name, or study and retrieved the result PDF-file from the DRS. We have currently implemented Statistical Parametric Mapping (SPM2) as default processing engine in the FGS, but other engines, e.g. AFNI, can be plugged-in as well. Processing consists of slice timing and head motion correction, anatomical co-registration, spatial smoothing, and time series analysis using t-test statistics.

Results and Breakthrough work:
We setup a testbed between Stanford Medical Center, Palo Alto, and CHLA/USC, Los Angeles, which are part of the Child Oncology Group (COG), a Grid with 22 of the 120 international pediatric hospitals. The average automatic fMRI processing of 100 cases, one session (64x64x40x80 image matrix) per case, was about 7 minutes, measured on a dual 2Ghz Opteron Server at CHLA/USC. The described design is currently implemented for COG Grid. We will report at the conference about our experience with the larger Grid installation.

Conclusion:
Grid technology provides methods for secure and efficient distribution of medical images using the Internet. DICOM format provides a standard image format. Here we demonstrate that by combining both standards one can establish an fMRI service which closes the missing link between image provider, e.g. Radiology, and image consumer of advanced imaging, e.g. Neurology or Neurosurgery. We conclude that Grid based fMRI services are an ideal solution to connect image providers which lack fMRI processing capabilities together with processing providers, fMRI expert centers. Such a concept may be the technical solution to overcome the current hesitation for clinical use of fMRI, caused by the technical burden and large variability in results due to missing standardized processing.

Co-chair: Gerhard Friehs, M.D.
Title: Associate Professor for Clinical Neurosciences (Neurosurgery)
Institution: Brown University, Providence, Rhode island
Time: *10: 50 – 11:10 AM*
Topic & Abstract:
Braingate - A Human Brain-Machine Inter-face
Abstract is not available

Speaker: Theodore W. Berger, Ph.D.
Title: David Packard Professor of Engineering and Neuroscience and Director, Center for Neural Engineering
Institution: USC
Time: 11: 10 – 11:30 AM

Topic and Abstract:
Implantable Biomimetic Electronics as Neural Prostheses for Lost Memory Function
Abstract is Not Available

Speaker: Mike Tyszka, Ph.D.
Title: Director, Magnetic Resonance Physics, Caltech Brain Imaging Center
Institution: *California Institute of Technology*
Time: 11:30 – 11:50 AM
Topic and Abstract:
Fact and Fiction: Artifacts in Functional Magnetic Resonance Imaging

Image formation and analysis in fMRI is a complex and often confusing process. Artifacts arising from the interaction of neurophysiology, image acquisition and statistical processing can be difficult to identify and minimize. In this talk we will cover the physiological, imaging and statistical processes underlying modern functional MR image formation in order to best understand the potential for artifacts and the most robust approaches to dealing with them.
Preferred Presentation Type: Oral
Section Preference: Biomedical Informatics and Physics
Keywords: Functional MRI, Magnetic Resonance Physics, Neurophysiology, Image Processing, Imaging Artifacts
Purpose: The purpose of this didactic presentation is to review the MRI physics, statistical image analysis and neurovascular physiology underlying BOLD fMRI in order to better to recognize and compensate for the most common artifacts which lead to inaccurate interpretation of fMRI data.
Methods: Examples from the literature and from 3T fMRI experiments in humans at the Caltech Brain Imaging Center will be presented illustrating various physiological, imaging and processing artifacts in BOLD fMRI. The latest theories of neurovascular coupling will be discussed. State-of-the-art pre-processing and statistical analysis will be reviewed in relation to fMRI artifact reduction. The effect of correlated physiological motion, large vessel signal contributions, task-dependent artifacts, signal dropout, image parameter selection and statistical analysis parameter choice will be covered in sufficient detail to allow the audience to design robust and reproducible BOLD fMRI protocols.
Conclusions: Accurate interpretation of BOLD fMRI requires an awareness of the mechanisms underlying neurovascular physiology, image formation and image analysis. The potential for over-interpretation of fMRI data can largely be avoided by careful imaging and analysis protocol design.
This work has not been submitted for publication of presentation elsewhere.

Speaker: David J. Dubowitz MD PhD
Title: Assistant Professor of Radiology; Associate Director, UCSD Center for Functional MRI
Institution: University of California San Diego
Time: 11: 50 – 12:10 AM
Topic & Abstract:
Beyond Brain Mapping: Using fMRI to Examine Cerebral Physiology & Metabolism

Abstract:
FMRI has the potential to go beyond simple mapping, and interrogate hemodynamic physiology and oxygen metabolism in the human brain in both health and disease. FMRI exploits the

sensitivity of MRI to local changes in the deoxyhemoglobin content - the Blood Oxygenation Level Dependent (BOLD) effect. Unfortunately, BOLD alone is difficult to interpret in a quantitative way; Recent work has shown that the magnitude of the BOLD signal varies significantly with baseline conditions, even for identical stimulus protocols. In addition, physiological interpretation is complicated as the BOLD effect depends on combined changes in three underlying physiological quantities: cerebral blood flow (CBF), cerebral blood volume (CBV) and cerebral metabolic rate of oxygen ($CMRO_2$). However, this complexity of BOLD also presents an opportunity to measure these basic physiologic parameters, particularly $CMRO_2$. For this we must combine BOLD-fMRI with other measurements to tease apart the different components. If we know how CBF and CBV are changing, the BOLD effect can be used to measure the change in $CMRO_2$. In short, combined MRI measurements yield much more quantitative physiological information than the BOLD signal alone. The ability to make reliable measurements of $CMRO_2$ change, and in particular the coupling of CBF/ $CMRO_2$, provides a unique probe of brain physiology and a potential marker of disease processes that affect cerebral energy metabolism.

Keywords:
Advanced MRI, physiology, oxygen metabolism, CBF, CBV

More details of talk:
This is a “looking into the future” talk.

Functional magnetic resonance imaging (fMRI) has revolutionized the study of the working human brain by providing a non-invasive tool for mapping brain activity. However, it's utility for clinical and neuroscience applications is not fully realized. FMRI has the potential to go beyond simple mapping, and interrogate hemodynamic physiology and oxygen metabolism in the human brain in both health and disease.

Honorary Luncheon Speaker: Dennis Malkasian MD PhD
Title: Clinical Professor, Division of Neurosurgery
Institution: David Geffen School of Medicine at UCLA
Time: (12:10 –12:35 AM)
Topic and Abstract:
Ontogenesis to Oncogenesis: Molecular Aspects and its Potential Clinical Application in Neuro-Imaging and Treatment of Brain Tumors.

In the normal morpho-neurogenesis of the nervous system there are a myriad of critical expressions of morphogens [e.g. SHH, Wnt, and HOX protein] and cascading activation of membrane receptors [e.g. tyrosine, serine and threonine phosphoprotein kinase receptors and cytokine receptors], ligands [e.g. PDGF, EGF, FGF, VEGF, and Eprhine], cellular cytoplasmic signal transduction pathways [e.g. TGF-SMAD, STAT, and JAK] and enhancing or silencing genomic expressions. Some of these processes upregulate cellular proliferation-growth [G-protein, Ras, MAPK, upregulating TOR and downregulating PTEN], differentiation [e.g Delta-Notch, Wilms Tumor suppressor gene, retinoblastoma suppressor gene, inhibitors of the mitogenic cell cycle check points] cell survival [e.g. NGF, BDNF and NT-3/NT-4], and apoptosis modulation [e.g. p53, MDM2, TNF, caspases, Bak, Bim, Bad, cytochrome - c and protein 14-3-3]. In normal embryogenesis EMT [Epithelial to Mesenchymal Transition; i.e. neuroepithelium to neural crest cells] and MET [Mesenchymal to Epithelial Transition; i.e. mesoderm during gastrulation to somites] is an ongoing process until organogenesis is completed. Celluar migration [Rho,

Rac, CDC-42, integrins and CAM's, netrin, robo, delta-notch, snail-slug homologies]. When some of these elements are inappropriately upregulated or downregulated along the biological timeline neoplasia may result.

Some of these errors have been studied in tumor development. The goal of the presentation is to provoke interest in identifying if the penumbra around a brain tumor is demonstrating molecular changes before gross or histopathological changes become apparent. Would there be a prognostic or therapeutic value in characterizing such processes? Answer, Yes.

Scientific Session VIII:
Neurophysiology: From the Lab Bench to Clinical Practice

Chair: V. Reggie Edgerton, Ph.D
Title: Professor and Vice Chair of Physiological Science; Professor of Neurobiology
Institute: Department of Molecular, Cellular, and Integrative Physiology; IBMISPS Board Member
Time: 2:00 – 2:20 PM
Topic and Abstract:
The role of Intramuscular Strain in Generating Force in Cats and Humans
V. Reggie Edgerton[1,2,3], Roy, Roland R.[1,3], Zhong, Hui[1,3], Sinha, Shantanu[4]
[1] Department of Physiological Science UCLA [2]Department of Neurobiology UCLA, [3]Brain Research Institute UCLA, [4]Department of Radiological Science UCLA

The properties of both the nervous system as well as muscle are highly responsive to the levels of activity. With respect to the neuromotor system, activity is directly reflected in the electrical events whereas muscle activity can be expressed as a mechanical event as well as an electrical event. We measured the electrical events representing both the motor neurons and the muscles. We will demonstrate major differences in activities between slow and fast muscles and between flexor and extensor muscles as well as from different species, including rats, monkeys and humans. Secondly, we will demonstrate the impact of in vivo activation of skeletal muscles during normal locomotion in the force velocity consequences of these activation levels. These in vivo force-velocity properties will be compared to in situ maximum force-velocity properties. These experiments demonstrate that the actual power generated by skeletal muscle during locomotion exceeds that which can be generated in situ with maximal stimulation during isotonic contractions. In another series of experiments we found that the architecture of the skeletal muscle is a major determinant of the physiological properties of the muscle, i.e. its force-velocity properties. And finally in vivo velocity of movement of specific segments of human muscle tendon complexes will be demonstrated and these properties will be correlated to the architectural features of muscle fibers, aponeuroses and muscle tendon complexes. Finally, we will describe how some of the strain properties within skeletal muscle complexes are modified as result of prolonged periods of reduced use and load bearing.

Speaker: Jiri Vrba, PhD
Title: CTO - Chief Technical Officer,
Institute: VSM Med Tech
Time: (2:20 – 2:30 PM)
Topic and Abstract:
Magnetoencephalography - A Tool for Assessment of Brain Function

Abstract: Electrophysiological neuronal activity in a functioning brain generates ionic currents, which in turn produce tiny magnetic fields outside the head. These fields can be measured and used to draw inferences about the state of the brain. The branch of science concerned with the measurement and interpretation of the brain fields is called MagnetoEncephaloGraphy (MEG). MEG, similar to electroencephalography (its older counterpart), operates on millisecond time scale, and is used for assessment of brain disorders or study functions of a normal brain. MEG systems are complex instruments incorporating superconducting SQUID sensors, sophisticated electronics, magnetic shielding, stimulation equipment, and processing software.

The small brain fields are overshadowed by magnetic noise from the environment. The MEG machines can reduce this noise by many orders of magnitude by utilizing noise cancellation techniques. In addition, it is necessary to separate signals generated by the targeted brain regions from the noise generated by other parts of the brain or by other electrically active tissues. Modern MEG systems have hundreds of sensors and such separation can be accomplished by utilizing correlations among them.

Brain scientist or surgeons are interested in current distribution within the brain, not in the measured magnetic fields on the scalp surface. Inversion of magnetic field into a 3D current distribution utilizes various mathematical simplification and/or assumptions and a wide range of methods for estimation of the brain currents are available. The presentation will review the MEG instrumentation, noise cancellation, and signal interpretation with emphasis on beamformer techniques originally developed in radar and underwater sonar work.

Keywords: magnetoencephalography, SQUIDs, noise cancellation, beamformers, epilepsy

Description of purpose: This is a review presentation of the relatively new brain imaging modality called magnetoencephalography (MEG). Objective of the presentation is to introduce MEG to the listeners who may have no familiarity with this imaging technology, to outline the principles of the method, explain instrumentation, and provide introduction to the MEG signal interpretation. The presentation will show the capability of MEG, will compare it with other functional modalities, and will indicate what type of information can be obtained from MEG measurements.

Methods: The methods underlining the emergence of the MEG imaging modality comprise combination of experimental and theoretical development. Each element of the MEG system is based on thorough theoretical understanding of the underlining physical principles and has undergone a painstaking experimental validation and modifications.

Results: The whole-cortex MEG development has progressed from early 64 channel systems to the present-day systems with more than 300 channels. The system are reliable and provide unique information, not available with other imaging modalities. The MEG software is also rapidly evolving, permitting more sophisticated interpretation of the MEG data, while striving to achieve simplicity required for clinical operation.

New or breakthrough work to be presented: The presentation will illustrate how a multidisciplinary effort to bring together diverse technologies, including superconducting magnetic field detectors, sophisticated multi-channel digital electronics, magnetic shielding, stimulation equipment, electromagnetic inversion problem, and processing software work together to provide a unique brain imaging modality.

Conclusions:

- Reliable, highly sensitive MEG systems are presently available and are routinely used in research and clinical environments.
- MEG operates in the presence of large environmental and body generated magnetic noise. This noise is successfully suppressed by a combination of hardware methods, synthetic noise cancellation, and spatial filtering.
- A wide range of signal interpretation methods are available.
- MEG systems are routinely used for presurgical mapping, epilepsy localization, and brain injury.
- MEG is applicable to presurgical language localization, dementia, memory disorders, learning disabilities, psychopharmacology, neuropsychiatry, and others.
- MEG has also been applied to unborn fetus. The fetal MEG is a new tool for assessment of neurological status of unborn fetuses and has potential to assist during high risk pregnancies and to provide diagnostics associated with infections, toxic insult, hypoxia, ischemia, and hemorrhage

Indicate whether work is being, or has been, submitted for publication elsewhere, and, if so, indicate how the submissions differ: Some parts of the work were submitted for publication elsewhere (principles of noise cancellation, principles and operation of beamformers, etc). However, since this is a review presentation, it was necessary to consolidates these published fragments into a cohesive story. In addition, several examples of MEG results (shown at the end of the presentation) have not been published before.

Speaker: William Suthering , M.D.
Title: Medical Director Epilepsy and Brain Mapping Program
Institution: Huntington Medical Research Institutes And Huntington Hospital
Time: 2:30 – 2:50 PM
Topic and Abstract:

MEG Spike Dipole Orientation in Temporal and Extratemporal Epilepsy

William W. Sutherling, M.D.[1,2,3], Warren S. Merrifield, B.S.[1,4], Adam N. Mamelak, M.D.[1,2,3,5], , Matthew L. Riggs, Ph.D.[4], Nancy P. Lopez, A.A., REEGT[1,2], Dinah Thyerlei, M.D.[1], John C. Mosher, Ph.D.[6], Richard M. Leahy, Ph.D.[7]
[1]Huntington Medical Research Institutes, [2]Epilepsy and Brain Mapping Program, [3]Huntington Hospital, Pasadena, California; [4]Loma Linda University, Loma Linda, California; [5]City of Hope Medical Center, Duarte, California; [6]Los Alamos National Laboratory, Los Alamos, New Mexico; [7]Signal Image and Processing Institute, University of Southern California, Los Angeles, CA.

KEY WORDS: **MEG, spike, dipole, partial epilepsy, surgery**

ABSTRACT. *Background.* EEG and MEG studies have shown an association between the orientation and location of epileptic spike dipoles. Spikes that points up occur in mesial temporal lobe epilepsy. MEG is predicted to be worse than EEG in orientation. We investigated spike dipoles in MEG of presurgical patients with mesial temporal lobe epilepsy versus extratemporal epilepsy, including lateral temporal and extra-temporal regions, to see if orientations differed.
Methods. 353 single spikes were measured on whole cortex MEG co-registered with MRI (MSI) in 24 patients. A single moving dipole in a sphere was applied to each spike.
Results. There was a statistically significant correlation between vertical location and orientation of MEG spike dipoles. Dipoles pointing up were inferior (r = -0.46, p=0.02). Mesial temporal dipoles did not point down or occur above sylvian fissure. Spikes pointing down or located above the sylvian fissure occurred only in neocortical or extratemporal patients.
Conclusion. Despite theory that MEG is worse than EEG to estimate dipole orientation, MEG spike orientation identified patients with partial epilepsy which was not mesial temporal.

PURPOSE. MEG is useful in presurgical evaluation of medically intractable partial epilepsy (Knowlton 1997; Mamelak 2002; Wheless 1999). Orientation of spike dipoles in EEG has clinical utility ((Ebersole 1990). Scalp EEG dipoles classify temporal versus extratemporal epilepsy: vertical in mesial temporal and radial in extratemporal epilepsy. MEG and EEG are complementary in theory; but, it is important to determine advantages in experiment. (Williamson 1981b) MEG should be more accurate than EEG for location, EEG for orientation (Stok 1986, 1987) and radial dipoles. We tested if MEG spike dipole orientation distinguished temporal versus extratemporal epilepsy.

METHODS. *Patients*. All sequential intractable partial epilepsy patients with MEG were studied over 2 years. All had 5 epileptic spikes, 24 patients (9 F, 15 M; 29.4 yrs ± 12.3). 18 had focal atrophy or gliosis. 15 patients had intracranial EEG. 11 had focal excision, with mean follow-up 24.6 months.

MSI. MSI used a 100-channel, 68-sensor site, whole head neuromagnetometer (VSM CTF Systems, Port Coquitlam, BC, Canada) with third-derivative gradiometers coupled to DC SQUIDs at 4K in a magnetically shielded room of μ-Metall™. System accuracy was 0.80 mm ± 0.6 by phantom and 1.4 mm ± 0.9 by dipole in a saline sphere. Baseline 200-milliseconds, sampling 1250 Hz per channel, bandpass 1.25 to 70 Hz. Equivalent current dipoles with best fit were calculated using a moving current dipole in a homogeneous sphere (Stok, 1986, 1987) with the downhill simplex (Press et al, 1992). Time points with residual errors greater than 20% variance were excluded. MRI: volume acquisition, T1-weighted; 0.3 Tesla Hitachi or 1.5 Tesla General Electric scanner. FOV 240 mm, 256x256 matrix, 2 mm axial slices no gap. MRI was co-registered with MEG

Statistics. The SPSS statistical package was used. Spearman rank correlation coefficients were calculated between the parameters. The level of significance (α) was p=0.05. Data were plotted in a scattergram for better visualization of trends.

RESULTS. Two main dipole "patterns" emerged visually in the studies as obviously different categories. One pattern showed temporal lobe dipoles, which pointed up. The other showed extratemporal dipoles, which pointed down. Figure 1 shows a scattergram of all 24 patients. The orientation of the spike dipoles is inversely correlated with location, with orientation on the x-axis and location on the y-axis. Each number in the scattergram reflects the patient number and shows a significant negative correlation for all patients between vertical location and vertical orientation, with upward pointing dipoles occurring more inferiorly ($r = -0.46$, $p=0.02$). The scattergram revealed further information. The scattergram was divided into four quadrants. All patients with temporal lobe epilepsy had mean spike dipole z-localizations less than 7cm. Sylvian fissure is about 7 cm above the origin of the coordinate system. It is not surprising that all temporal patients would have spikes at or below sylvian fissure. All but 3 temporal patients had dipole z-orientation greater than -.05. 3 patients with temporal dipoles pointing down had seizure onset in lateral cortex (Patients #5, 14 and 23).

NEW WORK. Comparison temporal versus extratemporal MEG spike dipole orientation.

CONCLUSIONS. This study showed a significant correlation between the orientation and the location of MEG spike dipoles. Inferior temporal dipoles pointed up. Dipoles higher in the brain tended to point down. This negative correlation makes sense anatomically for inferior temporal spikes. MEG spike dipole orientation added useful additional information to spike dipole location. MEG dipole orientation was useful and further studies are warranted to compare this utility to EEG's.

BEING SUBMITTED IN FULL LENGTH MANUSCRIPT TO EPILEPSIA.

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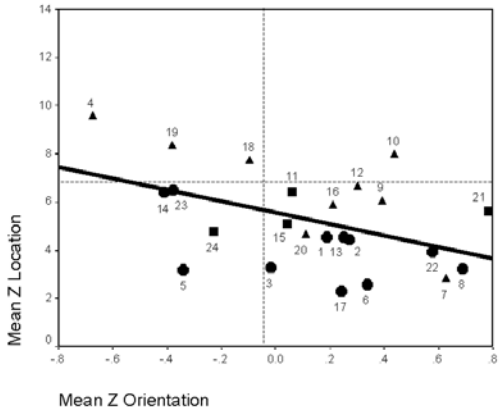

Figure 1. Scattergram of spike dipoles of 24 patients. Locations cm above origin. Solid line fit to points shows negative correlation (r = –0.46, p=0.02, two-tailed test). Dashed lines show temporal dipoles: z loc < 7cm and 73% had z-orient > -.05. Circles temporal, squares frontal, triangles extratemporal.

Speakers: Susan Bookheimer, Ph.D.
Title: Professor of Department of Psychiatry and Biobehavioral Sciences
Institution: UCLA School of Medicine, Ahmanson Lovelace Brain Mapping Center
Time: 2:50 – 3:10PM
Topic and Abstract:

Integrating Preoperative fMRI and awake Intra-operative Electrocortical Stimulation Mapping of Language

Pre-operative functional MRI can produce high quality maps of language and motor areas prior to surgery. However it is essential to validate any preoperative fMRI technique using standard procedures. When the goal of fMRI is to determine where functional areas are located with respect to the lesion (ie, intrahemispheric localization), the appropriate validation tool is electrocortical stimulation mapping (ESM). Furthermore, preoperative fMRI can inform the surgeon of likely functional areas prior to surgery. By combining the two techniques we can minimize the length of an intraoperative awake mapping procedure, using fMRI as a guide to hone in on probable language areas. This talk will describe procedures for preoperative fMRI, show how fMRI and intraoperative MRI navigation can be combined to direct ESM. I will describe how to use ESM to calculate sensitivity and specificity of fMRI maps. A series of case studies will demonstrate that many lesions that appear based on anatomy to be inoperable are resected safely using this combination of tools; I will also show conditions in which both ESM and fMRI can be misinterpreted to cause patient harm.

Co-Chair: Adam M. Mamelak, M.D.
Title: Co-Director of Pituitary Program
Institution: Neurosurgical Institute, Cedars-Sinai Medical Center, IBMISPS Board Member
Time: (3:10 – 3:30 PM)
Topic and Abstract:

Magnetoencephalography Directed Surgery for Neocortical Epilepsy

Adam N Mamelak, MD [1,2,3], Nancy Lopez REEGT [2] Massoud Akhtari, PhD[1],
W. William Sutherling, MD[1, 2,]

Institutions:
[1]Huntington Medical Research Institutes, Pasadena, CA
[2]Epilepsy and Brain Mapping Program, Huntington Memorial Hospital,
Pasadena, CA, [3]City of Hope National Medical Center, Duarte, CA
Object: Magnetoencephalography (MEG) and Magnetic Source Imaging (MSI) are increasingly utilized tools for pre-surgical localization of epileptic foci and areas of eloquent cortex. The utility of MEG must be carefully balanced against the high cost and technological investments required to perform these studies, particularly when less expensive alternative localization methods are available. To help elucidate the value of MEG, we critically reviewed our experience with whole-head MEG in the management of patients undergoing epilepsy surgery.

Methods: We identified 23 patients with suspected focal epilepsy that underwent whole-head MEG/MSI studies at our institution and subsequently had invasive intracranial electrode monitoring and electrocorticography (ECoG) to localize the zone of seizure origin for surgical resection. MSI results were retrospectively stratified into 3 groups by the number of interictal spikes (IIS) recorded during a 4 hour recording session: Class I (no spikes), Class II ($\leq$5 spikes), and Class III ($\geq$6 spikes). Class III was further subdivided based on the clustering density of IIS: Class IIIA= $\geq$4mm mean distance between IIS (i.e. diffusely clustered); Class IIIB <4mm mean distance between IIS (i.e. densely clustered). We analyzed these groups to determine to what extent the MSI results correlated with the ECoG -determined zone of seizure origin. In addition, we assessed whether or not the MSI study provided critical localization data and correlated with surgical outcome following resection. Statistical analysis of these correlations was also performed.

Results: Of the 40 patients studied, 23 had invasive monitoring, including 13 with neocortical epilepsy, 4 with mesial temporal lobe epilepsy, and 6 with suspected neocortical epilepsy that could no be clearly localized by ECoG. Depth electrodes were utilized in 9 cases, subdural grids in 9 cases, depth electrodes followed by subdural grids and strips in 4 cases, and intraoperative ECoG in 1 case. ECoG was able to localize the zone of seizure origin in 16/23 (70%) of these cases. In 11 of the 16 (69%) cases in which the ECoG was able to localize the zone of seizure

origin, the MSI IISs were classified as Class IIIB (many, dense) and regionally correlated to the MSI localization in all cases (i.e. same lobe). In contrast, no Class IIIB cases were identified when ECoG was unable to localize the zone of seizure origin. This difference trended toward but did not achieve statistical significance ($p < .0.23$), presumably due to the relatively small number of cases available for analysis. In 3 cases (all Class IIIB) MSI was used to focus invasive electrodes in locations that would not have otherwise been targeted and provided unique localization data not evident from other imaging modalities that strongly influenced the surgical management of the patient. The classification of MSI findings into subgroups and subsequent statistical analysis generated a model predicting that Class IIIB MSI data are likely to provide reliable information to guide surgical placement of electrodes, but all other groups do not provide reliable enough localization information to guide surgical decision-making.

Conclusions: MSI can provide unique localization information that is not available by other non-invasive methods. MSI appears most useful for cases of neocortical epilepsy. In particular, when an MSI study revealed six or more IIS densely clustered in a single anatomic location, then the MSI was highly correlated with the zone of seizure origin identified by ECoG. In these cases the MSI data may be useful to focus the placement of intracranial electrodes.

Third Day
Nov. 19th

Scientific Session VIII: Bioethics

Speaker: Shantanu Sinha, Ph.D.
Title: Associate Professor of Radiology
Institution: UCLA School of Medicine
Time: 8:22-8:40

Title: Structure-Function Correlation for the Musculo-skeletal system – an MR study.
Objective: To utilize the non-invasive, non-ionizing technique of Velocity encoded, Phase Contrast MR imaging to correlate the structure of the human multipennate soleus muscle in vivo, with the heterogeneous spatial distribution of functionality, determined in terms of peak shortening velocity during isometric contraction, in normal, atrophied and recovering subjects.

Methods: With both legs of the subject inserted into the head coil of a Siemens 3T scanner, with the right immobilized within a half cast, high resolution axial images of the entire lower leg were acquired for 3D reconstruction in a Vitrea workstation for structural information (N=12, normal,

N=12 ULLS). The subject was trained to exert isometric contractions timed to a computer generated audio cue. The output of an optical force transducer, imbedded in the sole of the cast, was used to measure force exerted and to gate the scan. It also provided a feedback to the subject via a LED bar-graph, both for timing and for consistency of force exerted as a fraction of MVC, and for subsequent force-strain analysis. For all subjects, 5 to 8 saggital, and 2~4 axial, segmented (4 views/segment), velocity encoded (VENC=10cm/s S/I), PC images were acquired with TE/TR/Flip angle of 5.3/11.3/30^{o}, 2 Avg, 22 cm FOV, 5 cm Sl.Thk, 20 phases/"R-R". The PC images were analyzed and mapped onto the anatomical images using an in-house built software.

Results: The 3D volume rendering of the soleus muscle revealed a complex internal structure, with the curved aponeurosis arising distally from the Achilles tendon covering the posterior aspect of the muscle and extending into its superior regions. A clear anterior protrusion from this aponeurosis, with its thickness and extent varying amongst subjects, extended along the longitudinal axis of the soleus into the superior region of the muscle. Extensive distribution of intramuscular connective tissue forms a somewhat diffuse structure. The distribution of velocity of tissues in the saggital and axial planes was clearly delineated into different domains, defined by different muscle fascicle orientation during a contraction. Those in proximity to the connective tissues associated with the insertion had in general about 1~2 cm/s higher velocity than tissues in proximity of the origin.

Conclusions: The detailed 3D structure of the anatomy as revealed in these studies, particularly in terms of possible fiber orientations, explained quite well the distribution of peak velocities in different parts of the triceps surae complex, providing new insights into the structure-function relationships of complex multi-pennate muscles.

Speaker: J. Patrick Johnson, M.D.
Title: Director of Cedars-Sinai Institute for Spinal Disorders
Time: 12: 20 – 12:40 AM
Topic & Abstract:
Image Guided Endoscopic Thoracic Spine Surgery

J. Patrick Johnson MD, John K. Stokes MD, Rod J. Oskouian MD, William W. Choi MD, and Wesley King MD

Introduction: Thoracoscopic spinal surgery has technical and anatomic challenges that result in difficult orientation with a 2-D imaging procedure in a complex 3-D structure. The purpose of this study is to evaluate the application of frameless stereotactic image guidance to thoracoscopic discectomy procedures.

Methods: Sixteen patients underwent image guided thoracoscopic discectomy procedures that combines these two technologies. Accuracy was determined by the registration (calculated) error and the actual navigation (intraoperative) error. Clinical outcomes and complications were reviewed.

Results: Accuracy determined by registration (calculated) and navigation (intraoperative) was 1.7mm and 1.2mm, respectively. The additional time required for the image guidance portion of the procedure was countered by the efficiency of the remaining procedure. Clinical outcomes and

complication were comparable with previous experience.

Conclusions: Image guided thoracoscopic spinal surgery can provide 3-D orientation to a 2-D imaging procedure that ultimately improves accuracy, efficiency and safety. Future developments in combining guidance technology with standard surgical procedures will likely continue.

Scientific Session XIV:
Vascular & Blood Flow Imaging

Chair: Elizabeth Bullitt, M.D.
Title: Professor of Neurosurgery; Board Member of IBMISPF
Institution: University of North Carolina
Time: 9:10 - 9:30 AM
Topic & Abstract

Evaluating the Emergence of Malignancy via Measures of Vessel Tortuosity visualized by MRA of Choroid Plexus Carcinoma in the Genetically Engineered Mouse

Elizabeth Bullitt[1], P. Anne Wolthusen[2], Lauren Brubaker[3], Weili Lin[3], Donglin Zeng[4] and [2]Terry Van Dyke

[1]Departments of Surgery, [2]Genetics, [3]Radiology, and [4]Biostatistics, University of North Carolina, Chapel Hill, NC, 27599.

It is difficult to assess the malignancy of tiny brain lesions noninvasively. A new approach in human patients employs magnetic resonance angiography (MRA) and calculates a quantitative, statistical measure of regional vessel tortuosity to produce a “Malignancy Probability” (MP). This approach delineates individual vessels and compares vessel shapes statistically between each test subject and a set of healthy controls. A limitation of MRA is that it cannot delineate vessels whose diameters are smaller than the voxel size used during acquisition. It is therefore unclear how well the MP can assess tiny tumors, since tiny tumors are rarely biopsied.

This study evaluates the ability of the human MP equation to distinguish between benign disease and tiny, emerging cancers in a genetically engineered mouse model of choroid plexus carcinoma (CPC). Ten healthy control mice, 10 mice with huge cancers, and 10 mice in a precancerous or early cancer stage underwent MRA. The MP for each test mouse was calculated via a statistical comparison with healthy controls. Results were assessed by whole-brain histology.

Results indicate that the MP equation correctly defined mice with choroid dysplasia as possessing benign lesions. By vessel count, neo-angiogenesis could not be detected until cancers had reached a volume of approximately 80mm^3. Vessel tortuosity measurements, however, correctly identified emerging malignancy in lesions larger than 0.3mm^3. We conclude that vessel tortuosity measurements show promise in correctly classifying small cancers as malignant, and that the same equation derived in humans appears valid for the mouse.
Supported by R01-EB000219 NIH-NIBIB

Purpose: Cancer-associated vasculature is abnormally tortuous. A quantitative, statistical analysis of vessel shape as defined from MRA therefore offers a new approach to assessing malignancy and to monitoring therapy. In a recent blinded study, 30 human brain tumors were imaged prior to total gross resection of each lesion. All lesions but one were correctly classified as benign or malignant on the basis of vessel shape. An interesting question is how large a cancer must be before vessel shape abnormalities become perceptible by MRA. The purpose of the current study is to begin to investigate this question by using a genetically engineered mouse model of choroid plexus carcinoma. These tumors reliably progress from dysplastic (benign) to microscopic

malignancies to huge cancers with an approximately known time course. An additional advantage of the mouse model is that whole brain histological information is available.

Methods: 20 TgT_{121};$p53^{+/-}$ mice, 10 with huge cancers and 10 with no cancer or with tiny cancers, underwent T1, T2, and MRA imaging. 10 healthy mice served as controls. All images were mapped into a common coordinate system. Tumor volumes were calculated from the gadolinium-enhanced T1 images of tumor mice and vessels were extracted from the entire brain of all mice. A region of interest (the tumor for lesions larger than $50mm^3$ and the ventricular system otherwise) was defined in each tumor mouse and mapped to the same mouse's MRA as well as to the MRA of each healthy animal. For each tumor mouse, vessel counts were made over the region of interest and normalized (z-scored) by vessel counts calculated from the control group. A "malignancy probability" (MP), derived from a statistical study of human patients, was also calculated for each tumor mouse. This MP employs two zscored tortuosity measures to produce a value between 0 and 100, with values of 0-40 indicating a low probability of malignancy, values 40-60 viewed as indeterminate, and values above 60 suggestive of malignancy.

Results: Although CPC tumors are neo-angiogenic, we were unable to perceive an increase in vessel count as determined by MRA until tumors reached a size of approximately $80mm^3$. Vessel tortuosity measurements, however, correctly identified emerging malignancy in lesions larger than $0.3mm^3$. For tumors larger than $0.3mm^3$, malignancy probability was not correlated with lesion size, as is consistent with the histology of these tumors.

New or breakthrough work: This work provides an important piece of information in a long-term project aimed at using statistical measures of vessel shape to assess disease. It is of particular interest that the same equation can be used across species.

Conclusions:
Publications: This work has been accepted for publication in the American Journal of Neuroradiology, but publication is likely to be many months in the future. This work has not previously been presented at any conference.

Co-Chair: Frank P.K. Hsu, M.D., Ph.D.
Title: Professor of Neurosurgery
Institution: Loma Linda University
Time: 9:30 - 9:50 AM

Topic & Abstract:
Perioperative Evaluation of Cerebral Vasculature

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Oral presentation-invited speaker
Section: Vascular and blood flow imaging

Peri-operative blood flow evaluations are important in the surgical management of cerebrovascular diseases. Advances in techniques have contributed to the improved outcome from cerebovascular procedures. Intra and extra cranial vascular surgeries can benefit from using such techniques in decision making and treatment effectiveness. Modalities including doppler ultrasound, micro-doppler ultrasound, conventional angiography, intra-operative angiography, thermal diffusion flowmetry, specific intraoperative MRI sequences (MRA, SWI, and DWI), CT angiography, and intravenous fluorescence angiography will be discussed. Surgeries such as carotid revascularization, aneurysm clipping, extra cranial to intracranial bypass, and arteriovenous malformation resection can become safer by utilizing these techniques. We review the current state-of-the-art modalities and status of peri-operative assessment of cerebral vasculature.

Keywords: intraoperative, perioperative, cerebral blood flow, cerebral vasculature

Speaker: Stephen Aylward, MD
Title: Director of Computer-Aided Diagnosis and Display Lab Associate Professor of Radiology, Surgery, and Computer Science
Institution: University of North Carolina at Chapel Hill
Time: 9:50 - 10:10 AM

Monitoring Tumor Margins During Treatment Using Automated MR to 3D Ultrasound Registration

Julien Jomier, M.S.
Computer-Aided Diagnosis and Display Lab
The University of North Carolina at Chapel Hill
Allen Friedman, M.D.
Chief of the Division of Neurosurgery
Duke University
Elizabeth Bullitt, M.D.
Professor, Division of Neurosurgery
The University of North Carolina at Chapel Hill

1. Abstract

Surgical plans often incorporate anatomic information from multiple modalities as well as molecular, functional, and atlas-based information. One challenge to the physician is how to precisely perform those plans as well as how to utilize pre-operative information when making intra-operative decisions.

We have developed an ultrasound annotation system that registers pre-operative MR/CT images with intra-operative 3D ultrasound images based on the vasculature and anatomic surfaces visible in them. Vascular networks are an excellent basis for registering medical images: they are well distributed throughout most organs, move as those organs move, exist at multiple scales, and are clearly distinguished by many imaging systems, e.g., MR, CT, and ultrasound. The proposed registration system is capable of accounting for organ deformations resulting from the surgical opening of a patient's abdomen, brain settling due to opening the skull, and organ changes due to radiation therapy.

In this paper we discuss three evaluations of the registration system: phantom studies, liver lesion RFA guidance experiments, and brain tumor resection guidance experiments.

2. Purpose

The broad goal of this ongoing project is to deploy a novel 3D image fusion method for registering pre-operative images with intra-operative images for image guided interventions. Our work is motivated by the realization that new in vivo imaging techniques can delineate tumor

margins based on molecular markers and gene expression and that to use those physiological images to guide a procedure, it is necessary to fuse them with intra-operative anatomical images. The fusion method presented in this paper enables such fusion.

3. Method

To align of pre-operative MR images with intra-operative ultrasound images, despite surgically induced deformations, we have developed a vessel-based registration strategy. It operates by hierarchically deforming vascular and surface models from MR images into alignment with corresponding features in ultrasound images. The components of the system are as follows:

1) Modeling vessel in the pre-operative data. Pre-operative model extraction supports intra-operative speed, accuracy, and automation. It is only necessary to extract geometric models from pre-operative data, i.e., to extract vessel centerlines and radiuses. Time can be taken to ensure that those pre-operative models are accurate and are likely to be prominent (sensitive and specific) in the intra-operative data.

2) Forming 3D ultrasound images from multiple intra-operative 2D ultrasound images. Magnetically tracking a 2D ultrasound probe, and calibrating magnetic tracker positions with the physical-world location of the ultrasound images enables physicians to acquire 3D ultrasound volumes by sweeping the 2D ultrasound probe over regions of interest.

3) Registering pre-operative models with intra-operative 3D ultrasound images. The process of deformable vessel registration uses the natural hierarchical relationship between vessels, as tree structures, to implement a coarse-to-fine optimization scheme. That is, the deformation process begins at "root" vessels and progresses along them and to their branches in a systematic fashion. This hierarchical process provides stability when dealing with noisy images, sparse images, and large deformations.

These components have been evaluated in a prototype surgical guidance system. In the first experiments, a gelatin phantom was scanned using CT and ultrasound. The accuracy with which markers could be reconstructed from the CT into the ultrasound data was measured. In the second experiments, liver MR data from subjects were registered with intra-operative 3D ultrasound images. The liver was chosen as the target organ because it can be accessed via ultrasound in volunteers. The third set of experiments is ongoing. Intra-operative 3D ultrasound images from brain tumor resections are being acquired and registered with pre-operative and post-operative MR images.

4. Results

In the phantom experiments, markers in the gelatin phantom (not used to perform the registration) were transcribed from the CT scans into 3D ultrasound images in less than 3 seconds with a mean error less than 2.0 mm and a maximum error less than 2.8 mm.

In the MR-to-ultrasound liver registration experiments, using 100 repeated re-registrations of the images from three subjects, points were transcribed from the MR into the ultrasound data to within 3 mm in 99% of the runs. We also added deformations of up to 2 cm to the already deformed ultrasound data, and still maximum transcription error was less than 3 mm in 89% of the runs.

The brain tumor resection experiments are ongoing. We are working with BrainLAB researchers and engineers to test the hypothesis that, when dealing with brain-shape changes during tumor resection, our VBR method can provide intra-operative registrations that require less time and are more accurate than the registrations provided by the manual registration method on the VectorVision system. Our system is being integrated with BrainLAB's VVLink research workstation. Ultrasound calibration and tracking systems are being updated. Phantom and liver experiments are being repeated using the updated systems. Patient data will be acquired once its validity has been established.

5. Conclusion

We have developed an automated method for maintaining the alignment of pre-operative MR images with intra-operative ultrasound images, despite the presence of deformations. Using this system, physicians will be able to integrate advanced pre-operative functional, molecular, atlas-based, and anatomical information into intra-operative decisions.

Speaker: Karen Tong, MD
Title: Assistant Professor, Radiology
Institution: Dept. of Neuroradiology Loma Linda University Medical Center
Time: (10:10 – 10:30 AM)
Topic & Abstract
CT and MR Perfusion for Assessment of Surgical Revascularization in Cerebral Ischemia

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Oral presentation-invited speaker
Section: Vascular and blood flow imaging

Chronic occlusive cerebrovascular disease results from various conditions causing stenoses and occlusions which may lead to intermittent neurological symptoms, either from hypoperfusion secondary to inadequate collateral circulation or because of emboli from the affected arteries. Although traditional cerebral angiography can reveal potential embolic sources and the presence of the collateral circulation, it can not readily determine whether that collateral is sufficient. CT or MR perfusion imaging allows for a rapid differentiation of these conditions so that further plans can be formed to either eliminate an embolic source or augment a low-flow status. Results obtained from these techniques can be interpreted based on the concepts of tissue demand, autoregulation, and
vascular reserve. While progressive occlusive disease increases the risk of major infarction in the distribution of the marginal perfusion, previous ischemic processes leading to tissue injury may have diminished the demand for blood flow to the territory in question. Therefore, a single measurement of cerebral blood flow may not be able to demonstrate true ischemia. In addition, cerebral blood flow may appear as adequate in a region distal to the occlusion because of both collateral flow and dilation of regional arteries to increase blood volume (autoregulation), both of which contribute to the vascular reserve. However, the vascular reserve may become compromised in the face of stressful conditions such as hypotension leading to cerebral infarction. In both of the above conditions, perfusion imaging in conjunction with “challenge” tests such as IV acetazolamide are needed to assess vascular reserve in the face of stress. These non-invasive techniques can identify those patients with chronic ischemia who are at high risk for

future stroke and who may benefit from cerebral revascularization procedures. The utility of CT perfusion and MR perfusion for revascualrization surgery will be reviewed. Examples of cases from Loma Linda University Medical Center will be shown, highlighting the potential benefit of these diagnostic tools in the management of patients with cerebral ischemic disease.

Keywords: CT, MR, Perfusion, Cerebral ischemia, Cerebral Revascularization

Speaker: Andreas Raabe, M.D.
Title: Associate Professor
Institution: Department of Neurosurgery Neurology and Neurosurgery Centre
Johann Wolfgang Goethe University
Time: 10:30 – 10:50 AM
***T*opic and Abstract:**
Prospective Evaluation of Surgical Microscope-Integrated Intraoperative Near-Infrared Indocyanine Green Video Angiography During Aneurysm Surgery

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Louis J. Kim, MD†
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Objective. We prospectively compared a new technique of surgical microscope-based indocyanine green video angiography (ICGA) with intraoperative or postoperative digital subtraction angiography (DSA).

Method. ICGA was performed during surgical clipping of 124 aneurysms in 114 patients in 187 procedures using a newly developed setup integrated into an operating microscope (Zeiss, Oberkochen, Germany). A microscope-integrated light source containing infrared excitation light illuminates the operating field. The dye is injected intravenously, and intravascular fluorescence from within vessels is imaged by a video camera attached to the microscope. Patency of parent, branching, and perforating arteries and clip occlusion of the aneurysm as shown by ICGA were compared to intraoperative or postoperative DSA findings.

Results. The results of ICGA corresponded with intraoperative or postoperative DSA in 90% of the cases. ICGA missed mild, but hemodynamically irrelevant stenosis that was diagnosed by DSA in 7.3% of cases. ICGA missed angiographically relevant findings in three cases (1 hemodynamically relevant stenosis and 2 residual necks, 2.7%). Two cases were clinically and surgically inconsequential; in the third case, a 4-mm residual neck may require a second procedure. ICGA provided significant information for the surgeon in 9% of cases, most of which led to clip correction.

Conclusions. Microscope-based ICGA is simple and provides real-time information about the

patency of vessels of all sizes and about the aneurysm sac. ICGA may be useful during routine aneurysm surgery as an independent form of angiography or as an adjunct to intraoperative or postoperative DSA.

Honorary luncheon speaker: Andrea K Scott, JD
Time: 12:45 – 1:05 PM
Topic and Abstract:
'STEM CELLS AND THE RESTORATION OF BRAIN FUNCTION: A HOBBESIAN CHOICE

Restoration of CNS function using transplanted cells has demonstrated the feasibility of cellular repair and regeneration of neural connections in the central nervous system (CNS). Recently, prominent scientists have proposed the use of stem cells for brain and other neurological repair. Opposition to this concept has come from diverse and otherwise seemingly unrelated segments of the American public who would outlaw virtually all research using stem cells and relating to cloning.

The principal reasons for this opposition include [1] aversion to destroying blastocysts or early stage embryos; [2] abhorrence of 'killing" a potential person as a result of embryo destruction; (3) concerns about tampering with the brain, which might alter the human persona or 'soul;" (4) legitimate ethical questions about unintentional medical consequences which remain unknown at present. In contrast, the potential benefits from the use of stem cells include arresting disease progression, restoring function, and prolonging as well as preserving life.

Historically, politicians have used faulty science and moral absolutism to justify political goals. Politicians continue to prey upon public fears and misconceptions to manipulate government funding of scientific endeavors. As a consequence, scientific progress has slowed dramatically. Considerable public pressure is motivating some politicians to rethink their opposition. More importantly, scientific data and the possibilities of stem cell research without embryo destruction have persuaded the American public that a thorough debate about stem cell research and cloning is warranted.

This discussion will focus on the following questions. [1] Is the scientific use of embryos equivalent to the destruction of human life? [2] Does restoration of cellular function in one area of the brain produce unintended consequences in another area? [3] Which parts of the brain are appropriate for the use of stem cells in restorative and medical procedures? [4] How will patients be chosen and who will establish these selection criteria? [5] Who should pay for these technologies, procedures and attendant rehabilitation regiments? Finally, as a society, we must decide where we choose to draw the line between restoration of lost function, improvement over baseline function and enhancement for its own sake.

For guidance, we might look to the British, who developed political consensus on issues pertaining to reproductive technologies via the Warnock Commission, which inspired the Human Fertilization Act of 1990 (HFE Act) and the Human Fertilization and Embryology Authority (HFEA). In stark contrast, the <?US has failed to produce legislation to set guidelines, an administrative body to oversee regulatory compliance, and funding to support stem cell research and related science within the field of reproductive technologies.

If you, as scientists and physicians, do not lead the charge in anticipating the need for public education and societal debate, regulations or judicial intervention based on inadequately informed opinions will severely retard our therapeutic options for decades to come.

Scientific Session IX: Brain Mapping in Neural Prosthesis & Brain Implants

Chair: Scott Frey, Ph.D.
Title: Director, Lewis Center for Neuroimaging & Assistant Professor of Psychology
Institute: University of Oregon
Time: 10:30 – 10:5 0 AM
Topic & Abstract:
Amputation and Cortical Reorganization: considerations for Neuroprosthetics

Abstract. This year in the United States alone approx. 10,000 people will lose all, or a significant portion of, one or both upper-limbs. Approximately half of these individuals will receive prosthetic services. Remarkably, only half of those fitted will use their prosthesis regularly. This high rejection rate is perplexing when one considers the widespread availability of sophisticated myoelectric technology that eliminates many of the discomforts associated with older mechanical limbs. Why are so few people adapting to these prostheses? One intriguing yet overlooked possibility is that this rejection rate represents a failure of the human brain to integrate the artificial limb into the existing body representation. In this talk I discuss research from cognitive neuroscience on the consequences of amputation and use of upper limb prostheses on functional organization of the cerebral cortex. I will identify several areas in desperate need of research, and argue that the success of the neural prosthetics effort depends critically on a more complete understanding of cortical plasticity.

Biography. Dr. Scott H. Frey (formerly published as "Scott H. Johnson" & "Scott H. Johnson-Frey") is currently Director of the Lewis Center for Neuroimaging at the University of Oregon and a member of the faculty in Psychology where he heads the human neuroimaging and transcranial magnetic stimulation laboratory. Scott received his Ph.D. in experimental psychology from Cornell University in 1993 for work on three-dimensional object recognition, and subsequently re-specialized in cognitive neuroscience techniques while on the faculty of the Center for Cognitive Neuroscience at Dartmouth College and Dartmouth Medical School.

website: **www.freylab.uoregon.edu**

Co-Chair: Joel Burdick, Ph.D.
Title: Professor of Bioengineering
Institution: Caltech
Time: 10: 50 – 11:10 AM

Topic & Abstract:
A Miniature Robot that autonomously Optimizes and Maintains Extra-cellular Neural Action Potential Recordings

Speaker: Yu-Chong Taii, PhD
Title: Professor of Electrical Engineering and Bioengineering
Institution: California Institute of Technology
Time: 11: 10 – 11:30 AM
Topic & Abstract:
Flexible Parylene Neural Prosthetic Devices

Flexible Parylene Neural Prosthetic Devices

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Motivated by the stringent requirements for a retinal implant device, the Caltech MEMS lab has developed a new Parylene technology especially to address three difficult issues that have hindered the device development in the past. First, as with any chronic implant, biocompatibility of the implanted materials, especially of those in direct contact with the patient's tissues and fluids, must be ensured. Long-term efficacy of the device must also be guaranteed, because revision surgeries are not tolerable; moisture can not penetrate the package over a period of decades. Secondly, of particular importance for the retinal prosthesis is the high-lead-count necessary to achieve truly useful vision. Thirdly, to ease implantation, the entire packaged system must be flexible such that it can be threaded through a small surgical incision. This technology takes care of all the three challenges by using a well-known biocompatible plastic polymer material called Parylene. More interestingly, however, we found that this technology simply provides a new way of making "flexible" device that could also benefit other fields like cortical implants and spinal cord implants. As a result, we have applied this technology to build silicon cortical implant probes integrated with flexible cables that can greatly simplify the construction and use of cortical implants. This work will describe the current state of this technology including subjects of material, technology, electrode integration, and IC packaging. The final product hopefully is a new generation of implant devices that are flexible, smaller, cheaper and better.

Key Words: Prosthesis and robotics, Neuroscience, implants, packaging

Presentation Preference: Guest Speaker

Section Preference: XIV: Brain Mapping Neural Prosthesis & Robotics 2

Speaker: Marco Iacoboni, MD/PhD
Title: Director, Transcranial Magnetic Stimulation Lab Ahmanson-Lovelace Brain Mapping Center Dept. of Psychiatry and Biobehavioral Sciences
Institute: Semel Institute for Neuroscience and Human Behavior Brain Research Institute; David Geffen School of Medicine at UCLA
Time: 11: 30 – 11:50 AM

The mirror neuron system and intention understanding

Mirror neurons are ventral premotor cells that fire when one makes an action and when one observes somebody else making the same action. They seem to provide a very simple neural mechanism for action recognition. Action recognition, however, has a special status with respect to recognition, for instance, of objects or sounds. Action implies a goal and an agent. Consequently, action recognition implies the recognition of a goal, and, from another perspective, the understanding of the agent's intentions. Mary is grasping an apple. Why is she grasping it? Does she want to eat it, or give it to her brother, or maybe throw it at me? I will present data that suggest that mirror neurons do not simply allow action recognition, they actually allow intention understanding. This is a key mechanism to predict the future actions of other people, an essential ingredient to successful social interactions. More generally, these data suggest that perception of action and intention of others is based on action simulation.

Speaker: Ramez Shehada, PhD
Title: Research Assistant Professor
Institution: Department of Biomedical Engineering
University of Southern California
Time: 11: 50 – 12:10 AM

The Smart Drain: A Surgical Drain with Sensors

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3. PRESENTATION PREFERENCE
Oral Presentation

4. SECTION PREFERENCE
Robotics

5. ABSTRACT TEXT

Vascular complications may occur after organ resection, transplantation, or trauma, and may compromise the survival of the organ and, in some cases, the patient. This necessitates the postsurgical localized monitoring of organs, especially those hypoxia-sensitive such as the brain. Current technology offers probes that require stitching to the tissue and therefore are not easy to apply or remove, which has been a key limitation to their wide acceptance in the medical field.

We have adapted a surgical drain to house sensors and act as a probe for monitoring the condition of adjacent tissue. This drain-probe provides the advantage of seamless integration into routine surgical procedures and simple attachment to the tissue by the drain's suction that would also act to clear the local fluids that otherwise may impede the sensors. The drain-probe can be used to monitor tissue oxygenation, perfusion, temperature, pressure, pH, humidity, as well as the biochemical composition of the drained wound fluids. We've called this drain-probe monitor the Smart Drain™.

Our first prototype included fiberoptic sensors to measure tissue oxygenation and was tested in-vivo on a pig model that was used to simulate hepatic artery thrombosis (HAT) and the interventional release of the thrombosis (reperfusion). The Smart Drain was able to promptly detect changes in the oxygenation of the liver under HAT and reperfusion conditions.

As the clinical interest is shifting from global to organ-specific monitoring, the Smart Drain may prove to be a valuable means for achieving this goal.

6. KEYWORDS
hypoxia, oximetry, surgical drain, monitoring, ischemia

Scientific Session X:
Neuro-mathematics & Modeling

Chair: Vittorio Cristini, Ph.D.
Title: Associate professor of Mathematics and Biomedical Engineering
Institution: University of California, Irvine, IBMISPF Board member
Time: 2:00 – 2:20 PM

Computer Simulation of Cancer and Chemotherapy

Not available.

Speaker: Vittorio Cristini, Ph.D.
Title: Associate professor of Mathematics and Biomedical Engineering
Institution: University of California, Irvine, IBMISPF Board member
Time: 2:20 – 2:30 PM
Morphologic Instability and Cancer Invasion

Vittorio Cristini,[1,2] Hermann B. Frieboes,[1] Robert Gatenby,[3,4]
Sergio Caserta,[5] Mauro Ferrari,[6,7] andJ ohn Sinek[2]
Abstract Purpose: A solidt umor embedded in host tissue is a three-dimensional arrangement of cells and extracellular matrix that acts as a sink of oxygen andce ll nutrients, thus establishing diffusional gradients. This and variations in vascular density and blood flow typically produce intratumoral regions of hypoxia andac idosis, and may result in spatially heterogeneous cell proliferation and migration.Here,we formulate the hypothesis that through thesemechanisms, microenvironmental substrate gradients may drive morphologic instability with separation of cell clusters from the tumor edge and infiltration into surrounding normal tissue. Experimental Design:We usedc omputer simulations and in vitro experiments. Results:We provide evidence that morphologic instability could be suppressed in vivo by spatially homogeneous oxygen andn utrient supply because normoxic conditions act both by decreasing gradients and increasing cell adhesion and, therefore, the mechanical forces that maintain a well-defined tumor boundary. A properly working tumor microvasculature can help maintain compact noninfiltrating tumor morphologies by minimizing oxygen andn utrient gradients. In contrast, antiangiogenic therapy, by increasing microenvironmental heterogeneity, may promotemorphologic instability, leading to invasive patterns even under conditions inwhich
the overall tumor mass shrinks.
Conclusions:We conclude that therapeutic strategies focused solely on reduction of vascular density may paradoxically increase invasive behavior. This theoretical model accounts for the highly variable outcome of antiangiogenic therapy inmultiple clinical trials.We propose that antiangiogenic strategies will be more consistently successful when aimedat ''normalizing'' the vasculature andw hen combinedw ith therapies that increase cell adhesion so that morphologic
instability is suppresseda nd compact, noninvasive tumormorphologies are enforced.

Co-Chair: John Sinek,Ph.D.
Institution: University of California, Irvine,Department of Mathematics
Time: 2:30 – 2:50 PM
Topic & Abstract:
How Much Does Limited Tissue Penetration Affect Anticancer Drug Efficacy?

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Abstract
Researchers such as Tannock and Jain have pointed out that an oft underestimated barrier to anticancer drug therapy is the inability of drug to penetrate deeply into tumoral tissue. The phenomenon seems to pivot about an inverse relation between "lateral" tissue penetration and "vertical" cell accumulation. We present research focused upon quantifying this effect based upon *in silico* modeling of tissue/cellular/sub-cellular level pharmacokinetics and pharmacodynamics. Our goals are

1. To demonstrate the inverse relationship between tissue penetration and cellular uptake;
2. To demonstrate the relationship between cellular uptake and cellular mechanisms such as P-gp efflux, lysosomal sequestration, and DNA-adduct repair;
3. To quantify the impact of penetration barriers by examining resultant cytotoxicity and cytotoxicity gradient in a model tissue section.

We model a tissue section 100-200 microns thick using a multi-compartment design, and simulate the delivery of drug from a vessel against one face of the section. We then use our own pharmacodynamics model to predict cytotoxicity throughout the section, based upon target (*e.g.*, DNA) exposure to drug. Model parameters are extracted from the literature, and initial simulations show agreement with experiments by Kuh *et al.* (1999) and Zheng *et al.* (2001) on histocultures of patient tumors. We are currently running our own experiments to produce more consistent data with which to fit the model, and will be verifying predictions on our own tumor spheroids. In the future the model will be incorporated in our lab's three-dimensional tumor simulator to predict tumor evolution and response to therapy.

Keywords: Biomathematics, Chemotherapy, Tumor, Simulation, Pharmacokinetics

Purpose
We model tissue/cell level drug pharmacokinetics and pharmacodynamics of cancerous lesion *in silico* to examine tissue penetration and cellular uptake. These two mechanisms are inversely related. Drugs that exhibit little penetration, like the anthracyclines, exhibit great cellular uptake, and vice-versa. Our goals are to demonstrate this inverse relationship, demonstrate the effect of tissue/cell parameters such as tortuosity of interstitial matrix and lysosomal drug affinity, and quantify the effect of penetration barriers by investigating cytotoxicity gradients throughout

lesion. The model will be incorporated into a multi-scale, three-dimensional tumor simulator that is concurrently being constructed and coded at the Cristini Biomedical Simulation Lab at UCI. Eventually, we expect that this simulator will be able to accurately predict tumor response to alternate therapies.

Methods

A tissue piece (slab) 200 microns thick with a blood vessel on one face is modeled using a multi-compartmental design. The compartments represent (1) interstitial volume, (2) intracellular cytosol, (3) intracellular target (DNA), and (4) lysosomes. With this model we can investigate the distribution of drug (and glucose and oxygen) *via* extravasation from the blood vessel, diffusion into the tissue slab, and uptake by cells. Tissue and cell parameters controlling diffusivity of drug through interstitium, cellular permeability, P-gp and MRP efflux pumps, lysosomal sequestration (anthracyclines), and DNA adduct repair (cisplatin) can be adjusted to vary the strengths of these phenomena. Thus, their impact on penetration and uptake can be investigated. The multi-compartment pharmacokinetics model is coupled with a pharmacodynamics model to demonstrate the final effect that drug penetration and gradients have on cell kill.

Initially, parameters are derived from experiments reported in the literature. As such, we do not expect the results to exactly predict *in vivo* or even *in vitro* (spheroids, histocultures) experiments. Still, relationships can be demonstrated and hypotheses generated. For example, increasing cellular permeability to a particular drug may increase cellular uptake, but at the expense of drug penetration. This can be easily demonstrated with our model. Currently, our associated wet-lab (UCI Chao Cancer Center) is performing a set of experiments to obtain a consistent set of parameters that should yield more accurate results. The model will be tested using spheroids grown by this lab.

Results

Simulations accord with results by Kuh *et al.* (1999) and Zheng *et al.* (2001) on histocultures of patient and xenograft tumors. In these experiments, drugs with high binding affinity to interstitial and cellular components demonstrate little penetration (paclitaxel and doxorubicin). Using parameters for these drugs results in simulations demonstrating large penetration gradients. Using parameters for cisplatin, however, results in simulations demonstrating little penetration gradient, something that has been noted in the literature. One important prediction of our model is that cell density is an important factor in penetration, with high density posing a greater barrier to drug penetration. In fact, Kuh's and Zheng's experiments show that penetration in xenograft tumor histocultures, which have higher cell density than patient tumor histocultures, is significantly poorer than penetration in the patient tumors. For more accurate results we are currently running our own experiments to produce more consistent data with which to fit the model, and will use our own tumor spheroids to compare prediction to experiment.

New Work

Although mathematical and *in silico* modeling of drug delivery and cellular uptake is not new, our work integrates model components into a higher order system in an attempt to predict lesion tissue response to anticancer drug. We do not simply model the cellular (monolayer) uptake and processing of drug molecules, nor only the diffusion and penetration of drug into tissue. Rather, we demonstrate the combined effect of these two processes, the effects of several parameters governing key cellular attributes and processes, and further demonstrate the cytotoxic effect on lesion tissue. As such, our model will be able to provide accurate prediction of lesion response to therapy.

Conclusions

We have constructed a temporospatial model of tissue and cell level anticancer drug pharmacokinetics and pharmacodynamics employing parameters derived from the literature. Our model predictions accord with experiments on histocultures found in the literature. Our associated wet-lab is performing experiments to provide a consistent set of parameters for the model. Once done we will test the model with our own spheroids. The model will be incorporated into our lab's three-dimensional tumor simulator and will be expected to eventually provide accurate and realistic simulation of clinical cases.

Concurrent Publication
The work is still in progress and will be submitted to a refereed journal. Its final form will differ from that presented at this conference in that it will be more developed.

Speaker: Hermann B. Frieboes, Ph.D.
Institution: University of California, Irvine, Department of Mathematics
Time: 2:50 – 3:10PM
Topic & Abstract:
An Integrated Computational/Experimental Model of Tumor Drug Response

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Presentation Preference: Oral presentation
Section Preference: Session 3
Keywords: Biomathematics, cancer, chemotherapy, simulation, model

Abstract Text:
Our goal is to enhance the efficacy of chemotherapy by enabling optimal treatment selection through the development of computer models that incorporate patient specific *in vitro* drug response information, biomarker profiling, and clinical imaging. We have integrated this concept with sophisticated mathematical models of tumor growth implemented via computer simulations. We have collected *in vitro* and *in vivo* tumor data relating to specific biological parameters that describe tumor treatment response. Parameters comparing two breast cell lines were obtained for Doxorubicin (Dox)-sensitive (MCF-7 WT) and Dox-resistant (MCF-7 40F) cell lines. Spheroid

drug response was measured via cell viability, metabolic activity, and proliferation endpoints. *In silico* simulations were developed by translating these endpoints into microphysical parameter values that uniquely characterize a specific patient's heterogeneous cancerous tissue and its response to chemotherapy. We incorporated the drug effect by using the cell proliferation endpoint for the mitosis parameter and the cell viability endpoint for the apoptosis parameter. Spheroid growth and drug response were modeled using two- and three-dimensional mathematical models of avascular tumor growth. Growth inhibition predicted by the computer model at different drug concentrations was compared with *in vitro* results. *In silico* therapy followed the same drug response trends as *in vitro*. The model also predicted drug response characteristics of drug-sensitive and drug-resistance tumor cells. Future computer simulations will take into account the complex dynamics of drug delivery to cancerous tissue *in vivo*, thus optimizing variables such as dosage, number and duration of cycles, and drug types to be used in combination.

Speaker: Valerie Trapp
Institution: Department of Biomedical Engineering – UC Irvine
Time: (3:10 – 3:30 PM)
Topic & Abstract:
The Utility of Vascularized Spheroids for Modeling Angiogenesis

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Abstract:
Angiogenesis is a key aspect of cancer progression and patient survival. We have produced three-dimensional spheroid co-cultures of cancer cell lines with microvascular endothelial cells (MVECs). In these models, lumen-like structures made up of MVECs penetrate the tumor spheroid, thereby creating a model of angiogenesis. Whereas numerous models for angiogenesis exist, few allow for the direct analysis of MVEC-cancer cell interactions. Our model of vascularized spheroids makes it possible to examine how cell lines of differing phenotypes modulate MVEC-mediated lumen formation, extracting data for a mathematical model. Another

advantage of our *in vitro* model is based on its spherical shape, which leads to radial gradients in nutrient exposure, hypoxia, and drug concentrations. Such gradients produce hypoxic and non-hypoxic populations that mimic in vivo tumor growth. These models were developed in part to extract data for an *in silico* model and test our hypothesis that spheroids derived from tumor cell lines expressing low levels of Thrombospondin-1 (TSP-1) would have greater endothelial cell invasion than those with high TSP-1. TSP-1 is the natural inhibitor of neovascularization and tumorigenesis in healthy tissue. It activates the CD36 receptor on endothelial cells, which can induce apoptosis. In order to extract data, TSP-1 expression by various tumor cell lines was characterized using western blotting and immunohistochemistry. Endothelial cell invasion was measured by staining MVECs with CD31 and CD105 reagents, and the cells were enumerated using light microscopy at a 200x field.

Preferred Presentation Type:
Oral Presentation

Keywords:
Biomathematics, Angiogenesis, Spheroid, Tissue Engineering, Predictive Oncology

Summary:
In order to extract information for our lab's mathematical model of tumor angiogenesis[1], we have developed a three-dimensional *in vitro* model of tumor angiogenesis which is reproducible in both size and shape. A novel characteristic of the model is that it is spherical, and therefore both drug and nutrient concentrations are homogeneous with respect to the circumference, but heterogeneous with respect to the radius. We begin by extracting data on Thrombospondin-1 (TSP-1), the natural inhibitor of neovascularization and tumorigenesis in healthy tissue.

Vascularized spheroids are fixed and characterized via immunohistochemistry (IHC). Endothelial cell invasion is measured by staining MVECs with CD31 and CD105 reagents, and the cells are enumerated using light microscopy at a 200x field. TSP-1 levels are measured via western blotting. We also use the novel homogeneous/heterogeneous characteristic of the spheroids to our advantage by removing successive layers of the spheroids through the differential trypsinization technique, described by Freyer et al. This technique, which "peels" successive layers of the spheroid, produces multiple populations of cells, which were exposed to different conditions. These layers produce semi-homogeneous populations we characterize in order to extract additional data for the *in silico* model.

TSP-1 is thought to mediate its antiangiogenesis effects by activating the CD36 receptor on endothelial cells, which can induce apoptosis signaling pathways. Our laboratory has grown spheroids from cell lines with differing expression levels of TSP-1. We expect that spheroids derived from cell lines with high levels of TSP-1 will contain fewer intraspheroidal MVECs after co-culture with MVECs than those with low TSP-1 levels.

In a 2004 paper, Timmins et al[2] described micro-vascular endothelial cells (MVECs) co-cultured with tumor cell spheroids producing branching networks of endothelial, luminal structures invading the tumor spheroid; however, no further paper has been published exploring the intricacies of angiogenesis process within a vascularized spheroid. We have extracted data from our vascularized spheroid model.

Accurate and versatile *in silico* and *in vitro* vascularized cancer models will provide engineers, doctors, and scientists with a more accurate picture of how cancer growth is influenced by stromal effects, which play a significant role in treatment. Knowledge gained from this model will enhance the development and study of angiogenesis in tumors, allowing us to understand cancer progression within a patient more accurately.

Work on TSP-1's interaction with MVEC in the vascularized spheroid model has been accepted for presentation at UC-Irvine's Annual Chao Cancer Center Retreat.

Scientific Session XI:
New Horizon

Chair: Shouleh Nikzad, Ph.D.
Title: Supervisor of In Situ Technology and Experiments Systems Section of NASA/JPL; Visiting Assistant Research Professor of Neurosurgery at USC-Keck School of Medicine; IBMISPS Board Member
Time: **(4:00 –4:20 PM)**
Topic & Abstract:
UV Imaging, Nanotechnology and Their Potential Medical Application

Ultraviolet (UV) imaging and spectroscopy have applications in many fields including astronomy, biology, neurosciences and criminology. Because many of the features and phenomena under study produce faint signals, the importance of detectors is common in all these fields. NASA has had a long-standing interest in ultraviolet and visible imaging technology for remote sensing. In recent years, NASA's trend toward more frequent and less costly missions has created a need for smaller and more capable instruments for astronomy, in situ planetary applications, as well as, atmospheric analysis and other remote sensing applications.

POSTERS:

Istvan Akos Morocz,M.D.
Brigham and Women's Hospital and
Harvard Medical School

Brain Mapping in the Human Cingulate Cortex

Presurgical mapping in the areas of the anterior cingulate zone (ACZ) is elusive and may require extensive intraoperative evaluation. Advances in paradigm design and data analysis in neuropsychological imaging can provide more detailed maps of this cornerstone area of human thinking. We report multi-focal ACZ findings in an event-related fMRI study about mental multiplication and estimation which were grouped into cognitive, emotional and motor regions. For example, the effect of numerical product size, a measure for number magnitude, was detected in the rostral portion of the ACZ, whereas closely adjacent a novel measure for conflict, our effect of task difficulty, was found where cognitive processes like attention allocation, decision making and problem solving reside. Moreover, numerical distance and task habituation were attributed to the ventral ACZ portion, perhaps pointing at processing of emotional elements like stress and number schism. Lastly, numerous preSMA and SMA foci in the dorsal ACZ were related to motor planning and execution. In short, we show a rich, spatially and temporally interwoven activation system evoked by mental arithmetic. Neurosurgical interventions in the concealed ACZ shall greatly benefit from the enhanced insight in the orchestration of frontal activation road maps gained with modern neuropsychological imaging tools.

Title: Bioluminescent Imaging in the *GFAP-luc* Transgenic Mouse Model of Neurological Damage and Disease

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Key Words: ***GFAP, bioluminescent imaging, neuronal damage, bacterial meningitis***

Abstract:

Bioluminescent imaging is a tool that can be used in transgenic (tg) animals to evaluate tissue damage, inflammation and the efficacy of drug treatment. We have generated a series of tg mice containing the luciferase reporter driven by promoters of genes activated during neuronal damage and inflammatory diseases. One of these models, using the glial fibrillary acidic protein (GFAP) promoter to drive luciferase (*luc*) expression, has been employed in the study of neuro-inflammatory disease. The expression of GFAP, the major intermediate filament protein of mature astrocytes, is considered to be a reliable biomarker of glial and neuronal damage. Rapid, direct, noninvasive, repetitive *in vivo* monitoring of the *Gfap-luc* biomarker during pathological conditions provides insights into the disease process and can assist in related drug discovery programs. *In vivo Gfap-luc* expression was examined by bioluminescent image analysis following *Streptococcus pneumoniae* infections in the CNS. Mice were infected with live *S. pneumoniae* by either lumbar or intracisternal inoculation. Strong bioluminescent signals were detected in the brain and spinal cords of infected mice as early as 24h after infection, regardless of the route of infection, suggesting the dissemination of bacteria or bacterial products along the CNS. The detection of *luc* activity in the CNS correlating with the progression of bacterial infection allows us to evaluate the effect of drug intervention in real-time in living animals. In addition, the administration of the neuro toxic agents MPTP and kainic acid were also found to increase *luc* expression in *Gfap-luc* mice.

Poster Session

The Human Frontal Eye Fields: Involvement in Visual Encoding and Preparation of Finger Movements

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Apart from the control of eye movements, the frontal eye fields (FEFs) are hypothesized to be involved in several other functions. For example, the FEFs are assumed to play an important role in visual encoding and the guidance of spatial attention. The FEFs are also assumed to establish a salience map of visual scenes to guide further detailed visual analyses of relevant objects. In a previous functional magnetic resonance imaging (fMRI) study, we investigated the interference of visual encoding and action preparation processes. In that study, we found evidence that the FEFs are engaged in both difficult visual encoding processes and preparation of finger movements. The aims of the present fMRI experiment were twofold. First, we wanted to investigate the potential overlap of activations elicited by eye movement control, visual encoding, and motor preparation in the FEF region. Second, the present experiment tested the salience map hypothesis by parametrically varying task difficulty during encoding. Participants performed three different tasks in counterbalanced order: A saccadic eye movement task for the individual localization of the FEFs, a difficult visual identification task, and a motor task where finger movements had to be selected and executed. The results confirm our hypothesis that the FEFs are involved in both saccadic eye movements and the two non-oculuomotor tasks. This finding demonstrates visual and more general motoric functions in a region of frontal cortex previously thought to be exclusively involved in oculomotor control.

Keywords: frontal eye fields, fMRI, visual encoding, finger movements, saccadic eye movements
Preferred presentation type: poster

Poster Session

ALSO SEE THE POSTER IN THE PDF FORM

Title : Development of a software for Transcranial Magnetic Stimulation : Potential Magnetic Field Mapping on Human Brain

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Abstract :
Transcranial Magnetic Stimulation use magnetic field to modify neuronal activity. The field is created by an intense current (about 10000 A) going through a coil during about several hundreds microseconds. The magnetic field crosses patient's head and creates depolarization on neurons. If TMS has many medical applications, it is still not well understood. Indeed due to human brain complexity and magnetic field properties, the precise area of stimulation is a main issue. To help pratician during his TMS session we propose to develop software, including coil design, coil placement, magnetic field computation and mapping on human head models. It shows that in some cases classical approximations can be wrong.\

Poster:

TITLE

Development of a Navigation System for Neurofiberscopic Surgery

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3. PRESENTATION PREFERENCE

Poster Presentation

4. SECTION PREFERENCE

Neurosurgery

5. ABSTRACT TEXT

Improved navigation and image guidance have the potential to reduce the invasiveness and risk of neuroendoscopic surgery; however, until recently, there have been few technologies available to intraoperatively track the tip of a typical neurofiberscope, or systems to guide such devices using pre-operative image data. In this work, we demonstrate a navigation approach using a commercially available electromagnetic sensor (Aurora®, NDI Canada) that can be inserted into the working channel of a standard flexible fiberscope. A skull-based approach is used to register pre-operative image datasets with the intra-operative tracker coordinate frame. Sensor coordinates, measured in real-time, are used to display the

position and orientation of the scope within these registered pre-operative MR images, using a research software platform called the 3D Slicer. Calibration phantoms and plastic models of the ventricular system are being used to evaluate the accuracy of the tracking and navigation system in the operating room. In addition, virtual endoscopic images are compared with the true endoscopic view captured by CCD camera, in order to validate the approach. This navigation system is highly significant for neuroendoscopic procedures using flexible fiberscopes, especially for paraventricular tumor biopsies and cyst wall fenestrations.

6. KEYWORDS

neuroendoscopy, fiberscope, navigation, virtual endoscopy, electromagnetic tracking

7. SIX-PARAGRAPH SUMMARY

Purpose

This work demonstrates an approach for navigating a fiberscope during neuro-endoscopic surgery in order to improve visualization and accuracy of scope placement, thereby reducing invasiveness and risk. Our aim is to augment the existing endoscopic camera view by dynamically displaying fiberscope tip position and orientation with respect to pre-operative MR images and surgical plans. The goal of this preliminary work has been to evaluate the feasibility of this approach using a commercially available tracking system and an open-source software environment for medical image visualization and analysis. The absolute accuracy of the tracking system and the accuracy of image registration are important validation metrics and are determined using calibrated phantoms.

Methods

A flexible fiberscope (Codman Steerable Endoscope 83-1340) has been instrumented with a 0.8mm outer diameter electromagnetic sensor inserted into the 1.2mm working channel and tracked using an electromagnetic localization system (Aurora®, NDI Canada). The single bare sensor coil provides 5 degree-of-freedom motion tracking in real-time. The Aurora® system is attached to a Linux-based PC, for which we have developed software drivers using the OpenTracker framework (http://www.studierstube.org/opentracker/). Medical images and relative fiberscope location are registered and graphically rendered using the 3D Slicer software interface (http://www.slicer.org).

System performance was measured empirically as follows:

1. Accuracy and repeatability of the tracking system were evaluated by placing the endoscope tip at calibrated points on a plastic phantom. The physical distance between the landmarks was known. The mean error between measured and known landmark spacing was computed over this workspace.
2. Navigation performance was evaluated using a rectangular acrylic plastic box—filled with water and containing a number of point landmarks. The box was imaged using Magnetic Resonance Imaging and placed within the Aurora's workspace. The image and tracker coordinate frames were manually registered by selecting point landmarks visible in the image volume, and by touching the corresponding landmarks on the box using a second calibrated Aurora probe. The endoscope tip was then guided to each of the landmarks using only the tracker coordinates and target landmarks visible on the graphical navigation display. The resulting placement error between the endoscope tip and the landmark was measured manually.
3. Navigation ergonomics within a plastic ventricle model were evaluated (shown on the right). A rapid prototyping system was used to produce this model from an image-based segmentation of a patient's ventricular system. MRI images of the patient's brain were registered to the plastic ventricle model using anatomical landmarks and the manual alignment scheme described in (2) above.

Results

The bare sensor coil has an outer diameter of 0.8mm and therefore easily fits into the 3 Fr. (1mm) working channel of the Codman scope. The manufacturer of the tracking system reports an RMS error of 0.80mm (95% confidence level = 1.4mm) and 0.30º (95% confidence = 0.60º), with their 5-DOF sensor at a radial distance of 300-400mm from the Aurora® field generator under ideal laboratory conditions. In our preliminary experiments, the magnetic localizer exhibited clinically relevant accuracy when tracking the fiberscope in the operating room. Localization accuracy was found to be similar to that reported by the manufacturer—RMS error of 0.89mm (95% confidence level = 0.17mm)—when tracking the fiberscope in the operating room (OR). Corresponding mean and maximum errors were 0.50 mm and 1.37 mm, respectively, within a typical surgical workspace for the instrument. Measurements were taken from 96 pairs of points—each pair spaced 50mm apart—around the head of a volunteer subject as he lay on the surgical table. Navigation of the scope can be significantly enhanced by the spatial information provided by the visualization interface, which displays both a roadmap image showing the position and orientation of the scope within the pre-operative image volume, as well as a virtual endoscopic view.

New or breakthrough work to be presented

Optical tracking of rigid endoscopes is relatively straightforward; however, to the best of our knowledge, position and orientation tracking of the tip of a flexible neuroendoscope has not been demonstrated previously. Compact electromagnetic sensors that are small enough to fit inside the working channel of a neuroendoscope (i.e., approximately 1mm diameter) have not been available until recently. This work integrates such a sensor with image registration and visualization software to demonstrate a new navigation approach that will allow surgeons to directly visualize and maneuver a fiberscope using pre-operative images and surgical plans during an intervention.

Conclusions

A new navigation system for neurofiberscopic surgery has been demonstrated. This navigation system is highly significant for procedures, especially for paraventricular tumor biopsies and cyst wall fenestrations as it allows the surgeon to directly visualize and guide the position and orientation of the scope within pre-operative image data. We have measured satisfactory localization performance using a commercial electromagnetic tracking device; however, accuracy may be improved with additional shielding of the sensor coil and better placement of the field generator in the OR. Registration of pre-operative images is critical for overall accuracy and utility of the navigation system. Deformation of the ventricles will occur intra-operatively, thus degrading this registration and overall accuracy. We will evaluate the significance of this shift during clinical trials with the tracked fiberscope, by carefully comparing optical and virtual endoscopic images acquired during the procedure. This approach may encourage the use of registered multi-parametric image datasets and more complex surgical plans that can also be visualized dynamically during surgery, thus leading to new methods and applications.

Prior Publication or Presentation of this work: None.

1. PAPER TITLE

Development of a Navigation System for Neurofiberscopic Surgery

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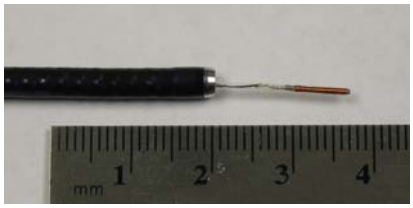

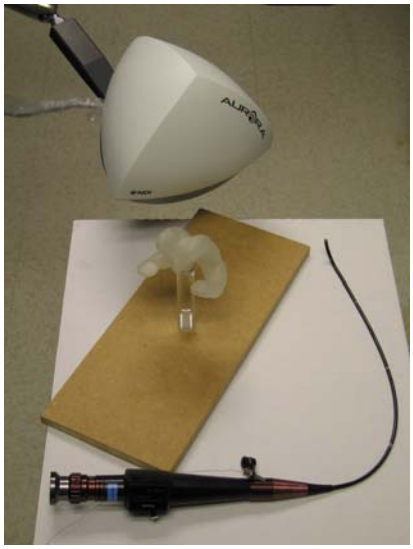

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Prior Publication or Presentation of this work

None.

Simulation of Transcranial Magnetic Stimulation : Brain Mapping of Magnetic Field Potential

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***Abstract*— Transcranial Magnetic Stimulation (TMS) modifies neuronal activity. The magnetic field is created by an intense current (about 10000 Amp) going through a coil during several hundreds micro seconds. It crosses skin and skull, depolarizing brain cells in particular in the cortical grey matter. If TMS has already many medical applications, the mechanism of action is still not well evaluated. Due to both brain complexity and magnetic field properties, the knowledge of stimulation volume, in clinical conditions, is a main issue. To help physicians to plan and to realize a TMS session, we developed software including coil design and positioning and magnetic field mapping, on a patient-based head model. Preliminary results showed that it gives pertinent information which could be of interest in clinical environment. The prospects are to integrate more biophysical data in order to simulate TMS accurately allowing clarifying the clinical effects.**

Keywords : Transcranial Magnetic Stimulation, Coil Design, Magentic Field Computation, Field Mapping
Presentation type : Poster **Section preference** : III

I. Description of purpose

TMS is a technique for modulation of brain activity. Neurons are stimulated by an electric current yielded by the magnetic field of a coil localized above the patient's head [1]. The use of magnetic field instead of direct electric field or electrical current makes TMS painless [2]. In addition TMS is non-invasive and can be used in ambulatory conditions.

Applications in medical care and research domains are proposed [3]:

- brain mapping
- psychiatry : treatment of mood disorder and schizophrenia
- treatment of epilepsy
- treatment of severe chronic pain

Nevertheless TMS is still empiric and physicians have to make many approximations to set coil position and orientation according to the clinical objective. Several parameters influence the positioning settings of coil: coil shape, magnetic field spreading, and head and brain shapes of each individual case, in particular the distribution of gyrus and sulcus.

A. Coil shape

Coil design is a major issue for TMS: the magnetic field shape is given by the Biot & Savart Law; the design of coil winding leads the shape of magnetic field. So manufacturers proposed different coils [1]:

- simple coil : circular winding
- 8-shaped coil : similar to two simples coils (currents circulating in opposite ways)
- double cone coil: an 8-shaped coil with an angle between the two wings (wing angle).

B. Magnetic Field Focalization

The 8-shaped and the double cone coils are expected to have better focalization. Comparing modulus of magnetic field potential generated by simple and 8-shaped coils, in a plane parallel to the coil plane, the field is stronger below the intersection of the two wings of 8-shaped coil (Fig 1)

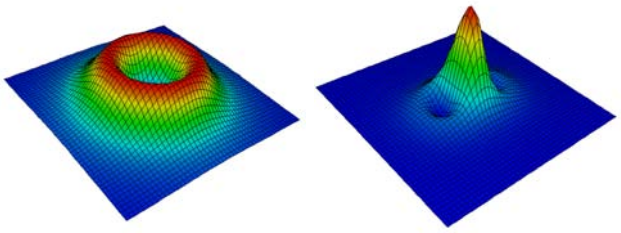

Fig. 1. Normalized magnetic field potential modulus on a plane parallel to the coil plane for circular and 8-shaped coils

C. Physician considerations

Eight-shaped coil is preferred in some applications expecting a sharp strong field along an axis perpendicular to coil plane going through its centre. Simulation tools set the hot spot of stimulation at the intersection of this axis and patient cortex [4] [5]. This could be inaccurate in some cases, as the distance between coil and head and the orientation of coil are not always taken into account. We proposed to develop a TMS simulator to analyze the influence of these parameters.

II. Method

A TMS simulation session can be divided into three parts:

- the definition of coil design
- the definition of stimulation parameters
- the definition of coil position above head

Having these parameters defined, simulation can be launched and potential magnetic field can finally be mapped on a patient brain model.

A. Coil Design

In order to take into account the coil design, we chose a model using 3D-parametrical equation of coil winding [6]. With the Biot & Savart law, it allowed to numerically compute magnetic field at any point of empty space.

B. Parametrisation

The coil model can be described by different parameters, e.g for a simple coil by radius and for a double cone coil by radius and by wing angle. We developed a Graphical User Interface to set interactively the model. Three parts composed the interface:

- a tree (Fig 2, top left), displaying a hierarchical view of parameters, allowing to browse and quickly find the one to modify, e.g. coil (radius, wing angle; set together) parameters (Fig 3)
- a panel (Fig 2, bottom left) displaying the parameters of selected group.
- a graphical window, using OpenGL (Fig 2, right), displaying the simulation scene : coil, brain mesh and magnetic field mapping.

Others parameters, e.g. intensity or coil position and orientation, can be set.

C. Head Model and Mapping

To fit at best the magnetic field mapping to each real case, i.e. a patient, we used MRI data to generate a surface mesh of patient's head using Marching Cubes Algorithm [7]. We computed magnetic field for each vertex of mesh and displayed it.

III. Results

The magnetic field mapping simulation of a double cone coil showed the influence of wing angle direction on focalization. When the angle opening looks at the head there is no focalization (Fig 2). The focalization is optimized with

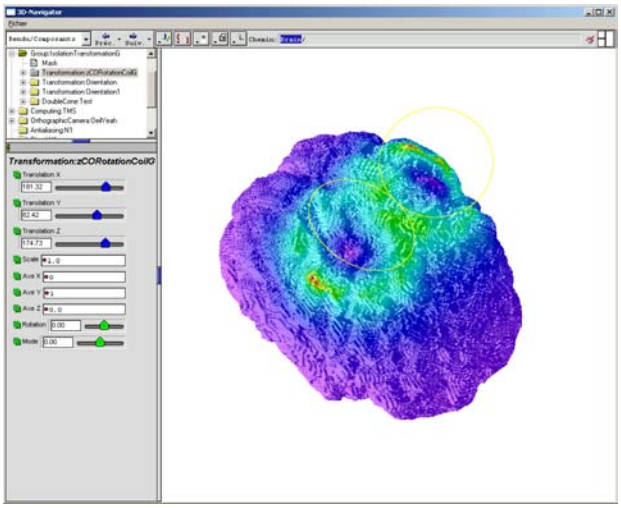

Fig. 2. Mapping of Magnetic Field Potential Modulus generated by Double Cone Coil; opening of wing angle looking at the head

the coil in an opposite way, reversing the orientation of the wing angle (Fig 3)

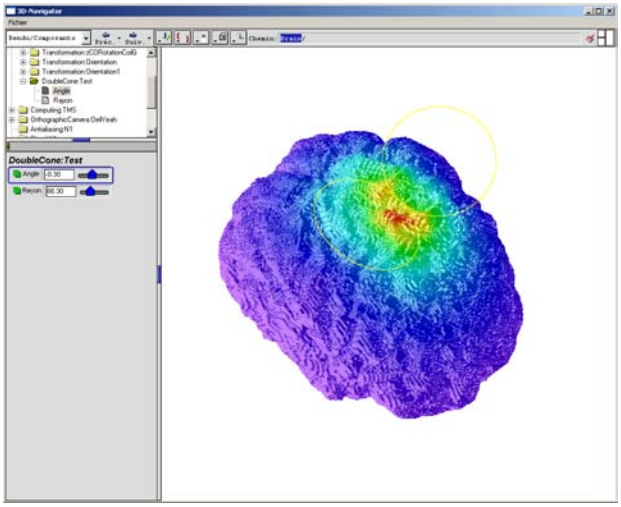

Fig. 3. Mapping of Magnetic Field Potential Modulus generated by Double Cone Coil; wing angle reversed

IV. Conclusion and Future prospects

Results, selected among the whole simulations, show the interest of simulating tools of TMS effects, at least from a biophysical point of view. This could open the outlook for a better analysis of clinical effects.

TMS simulation software has integrated a preliminary work into a friendly and easy tool, and by now an upgrade is in progress:

- to display the distance between coil center and head surface during coil placement step
- to upgrade tools to define coil design
- to add a finite element based module to compute electric field into patient's head in order to display it directly on cortex
- to reduce mesh size (today about 1 million vertex) using decimation algorithm

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